EFFECT OF THYROID DISORDERS ON NERVE CONDUCTION STUDIES IN FEMALES

Dissertation submitted to

THE TAMILNADU DR.M. G. R MEDICAL UNIVERSITY

CHENNAI- 600032

In partial fulfillment of the requirement for the degree of

Doctor of Medicine in Physiology (Branch V)

M. D. (PHYSIOLOGY)

APRIL 2015

DEPARTMENT OF PHYSIOLOGY

TIRUNELVELI MEDICAL COLLEGE

TIRUNELVELI- 11.

CERTIFICATE

This is to certify that the dissertation entitled, "**EFFECT OF THYROID DISORDERS ON NERVE CONDUCTION STUDIES IN FEMALES**" by DR.K.BALASUBRAMANIAM Post graduate in PHYSIOLOGY (2012-2015), is a bonafide research work carried out under our direct supervision and guidance and is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, for M.D. Degree Examination in Physiology (Branch V), to be held in April 2015.

Dr. L.D.THULASI RAM MS. (ortho)
Dean
Tirunelveli Medical College
Tirunelveli-11.

Dr. B. SUJATHA M.D .D.A.,
Professor and Head
Department of physiology
Tirunelveli Medical College
Tirunelveli- 11.

DECLARATION

I solemnly declare that the dissertation titled "**EFFECT OF THYROID DISORDERS ON NERVE CONDUCTION STUDIES IN FEMALES**" is done by me at Tirunelveli Medical College hospital, Tirunelveli.

The dissertation is submitted to The Tamilnadu Dr. M.G.R.Medical University towards the partial fulfilment of requirements for the award of M.D. Degree (Branch IV) in Physiology.

Place: Tirunelveli

Date:

Dr. K. BALASUBRAMANIAM
Postgraduate Student,
M.D (Physiology)
Department of Physiology,
Tirunelveli Medical College
Tirunelveli.

TIRUNELVELI MEDICAL COLLEGE

INSTITUTIONAL RESEARCH ETHICS COMMITTEE

TIRUNELVELI, STATE OF TAMILNADU, SOUTH INDIA PIN-627011
91-462-2572202,257,91-462-2572944, 91-462-2574200, 91-462-2573033-38
online@rediffmail.com, tirec@rediffmail.com, www.tirec.ac.in

ERTIFICATE OF REGISTRATION & APPROVAL OF THE TIREC REF NO: 503/PHY/2014/10

ROTOCOL TITLE: EFFECT OF THYROID DISORDERS ON NERVE CONDUCTION STUDIES IN FEMALES.

AME OF PRINCIPAL INVESTIGATOR: Dr. K.Balasubramaniam, MBBS., DLO.,
ESIGNATION OF PRINCIPAL INVESTIGATOR: Post Graduate in MD Physiology
EPARTMENT & INSTITUTION: Department of Physiology, Tirunelveli Medical College.

ear Dr. K.Balasubramaniam, The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your plication during the IEC meeting held on 24.05.14.

E FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

.	TIREC Application Form	☐
.	Study Protocol	☐
.	Department Research Committee Approval	☐
.	Patient Information Document and Consent Form in English and Vernacular Language	☐
.	Investigator's Brochure	☐
.	Proposed Methods for Patient Accrual Proposed.	☐
.	Curriculum Vitae of the Principal Investigator	☐
.	Insurance /Compensation Policy	☐
.	Investigator's Agreement with Sponsor	☐
.	Investigator's Undertaking	☐
.	DCGI/DGFT approval	☐
2.	Clinical Trial Agreement (CTA)	☐
3.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
4.	Clinical Trials Registry-India (CTRI) Registration	☐

E PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 2weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
   d. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IEC, only then can they be implemented.
   e. Approval for amendment changes must be obtained prior to implementation of changes.
   f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g. Any deviation/violation/waiver in the protocol must be informed

ANDS APPROVED UNDER SEAL

Dr.N.Dhanapalan MD
Registrar, TIREC
Tirunelveli Medical College, Tirunelveli – 627011
State of Tamilnadu, South India

Dr.V.Ramesh Kumar MD DM
Member Secretary, TIREC
Tirunelveli Medical College, Tirunelveli – 627011
State of Tamilnadu, South India

ACKNOWLEDGEMENT

I sincerely express my heartful gratitude to the beloved Dean, Prof **Dr. L.D.Thulasiram M.S.,(ortho)** Tirunelveli Medical College, Tirunelveli for all the facilities provided for the study.

I am thankful to **Dr. N.Thirumani Pandian M.S., M.ch,** Vice Principal, Tirunelveli medical college for his encouragement during the study period.

I take this opportunity to express my profound gratitude to **Dr. B . Sujatha M.D., D.A**., Professor and Head, Department of Physiology, Tirunelveli Medical College, whose kindness, guidance and constant encouragement and support enabled me to complete this study.

I am greatly indebted to **Dr. R. Saravanan MD.DM** Professor and Head, Department of Neurology and **Dr. Radha MD.DM**, Assistant professor, Department of Medical Neurology, Tirunelveli Medical College for their expert guidance in midst of their workload all through this work.

I thank **Professors and Heads, Department of Medicine and Surgery**, Tirunelveli Medical College for providing the subjects for the study.

I am highly obliged to all Assistant Professors, Department of Physiology, Tirunelveli Medical College, for their encouragement, and

corrective comments during the research period.

My special thanks are due to my postgraduate colleagues, Department of Physiology, Tirunelveli Medical College, for never hesitating to lend a helping hand throughout the Study. I am thankful to all other teaching and nonteaching staffs of Department of Physiology, Tirunelveli Medical College.

I thank **Mr. Heber**, senior clinical scientist, Dr Agarwal's centre for translational research for helping me in statistical analysis of the study.

I sincerely deliver my thanks to all the subjects participated in the study who are the backbone for the success of the study.

Last but not the least I am indebted to my wife **DR. C Meenakshi**, my children **B.Subakrishna and B.Navaneeth Kumar ,** my parents and family members not only for their moral support but also for tolerating my dereliction of duty during the period of my study.

Finally I thank the Almighty for without Him nothing would have been possible.

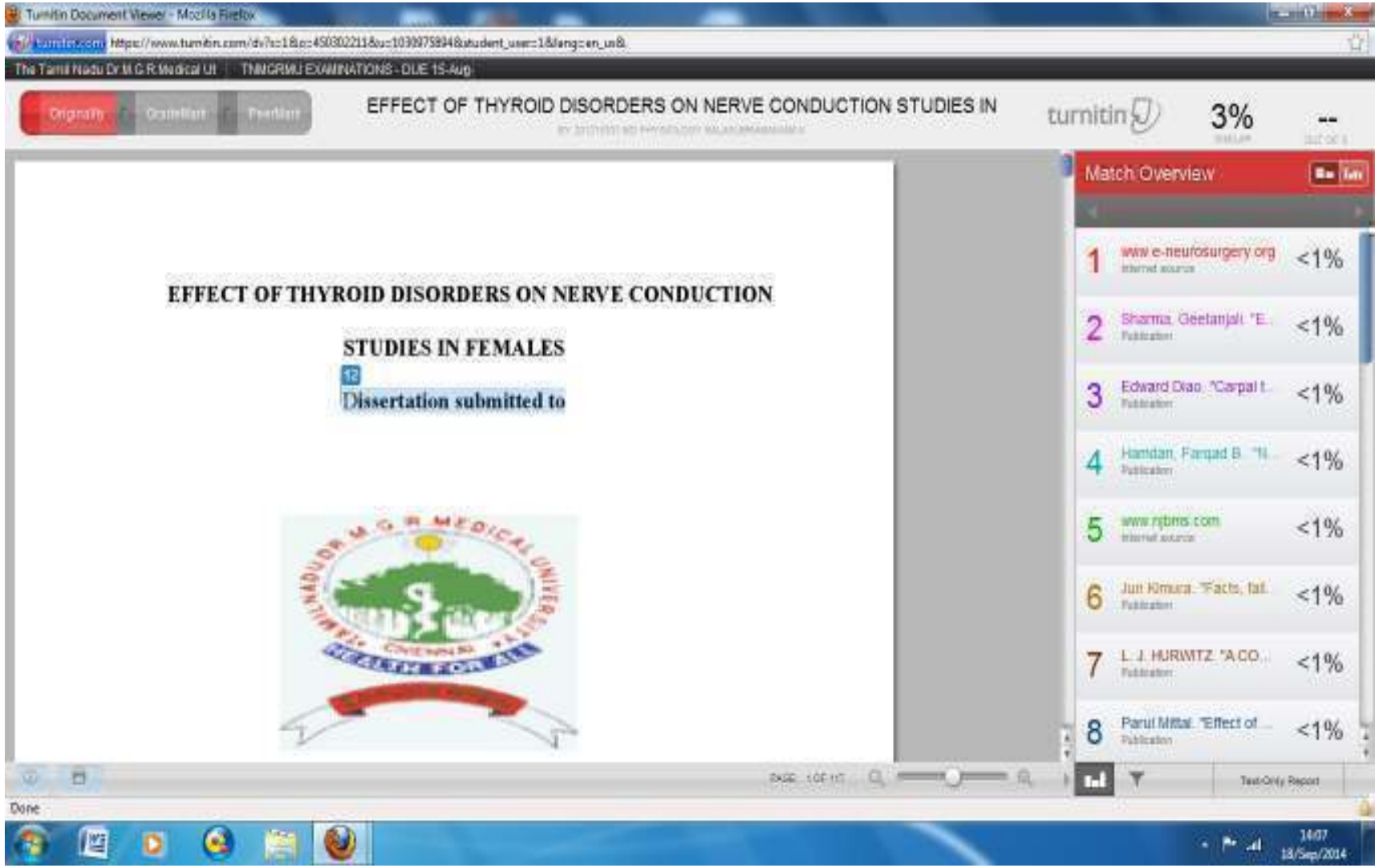
turnitin

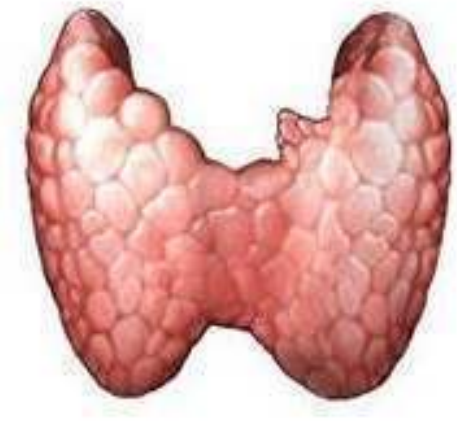
Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	201215301.md Physiology BALASU...
Assignment title:	TNMGRMU EXAMINATIONS
Submission title:	EFFECT OF THYROID DISORDERS..
File name:	Main_Content.doc
File size:	1.69M
Page count:	117
Word count:	21,588
Character count:	119,592
Submission date:	18-Sep-2014 12:12PM
Submission ID:	450302211


Turnitin Document Viewer - Mozilla Firefox
The Tamil Nadu Dr M G R Medical Ut
TNMGRMU EXAMINATIONS - DUE 15-Aug
EFFECT OF THYROID DISORDERS ON NERVE CONDUCTION STUDIES IN
turnitin
3%
--
EFFECT OF THYROID DISORDERS ON NERVE CONDUCTION
STUDIES IN FEMALES
Dissertation submitted to
Match Overview
1 www.e-neurosurgery.org <1%
2 Sharma, Geetanjali. "E... <1%
3 Edward Diao. "Carpal t... <1%
4 Hamdan, Farqad B. "N... <1%
5 www.rsbms.com <1%
6 Jun Kimura. "Facts, fal... <1%
7 L. J. HURWITZ. "A CO... <1%
8 Parul Mittal. "Effect of ... <1%
Done



EFFECT OF THYROID DISORDERS ON NERVE CONDUCTION STUDIES IN FEMALES

CONTENTS

ABBREVIATIONS USED

TSH	-	Thyroid Stimulating Hormone
TRH	-	Thyroid Releasing Hormone
T 4	-	Thyroxine
T 3	-	Triiodothyronine
THR	-	Thyroid Hormone Receptor
MIT	-	MonoiodoTyrosine
DIT	-	DiiodoTyrosine
Na^+- K^+ pump	-	Sodium potassium pump
RMP	-	Resting Membrane Potential
SNAP	-	Sensory Nerve Action Potential
CMAP	-	Compound Muscle Action Potential
DL	-	Distal Latency
CV	-	Conduction Velocity

EFFECT OF THYROID DISORDERS ON NERVE CONDUCTION STUDIES IN FEMALES

Balasubramaniam K, Sujatha B, Parvatharani R

Introduction: The magnitude of thyroid disorders are increasing globally. In India also there is an increasing incidence even though India is in post iodination phase. Most commonly the thyroid disorder is due to autoimmune pathology. Thyroid disorders affect all systems of the body including nervous system. The affection of neuromuscular problems includes proximal myopathy and various peripheral neuropathies. The early detection of peripheral neuropathy before clinical manifestations using electrophysiological methods helps in prevention of morbidity associated with the complications. **Aims and Objectives:** This study was carried out to evaluate the changes in the abnormalities in nerve conduction parameters in thyroid disorders and to find out the magnitude of neuropathies. **Materials and Methods:** The study was conducted at Tirunelveli Medical college hospital after ethical clearance. Proforma was filled in to follow the inclusion criteria and exclusion criteria. 22 hypothyroid,18 hyperthyroid and 25 normal individuals were selected for the study and written informed consent was obtained. The sensory conduction was performed in sural, median and ulnar nerves and motor conduction in tibial, median and ulnar nerves of left side using RMS EMG EP MARG II equipment. **Results and discussion:** The study found out predominant sensory involvement in both groups. Sensory neuropathy was present in 45.4 % and 61 % of hypothyroid and hyperthyroid individuals respectively. Sensorimotor neuropathy was present in 9.1 % and 5.5 % of hypothyroid and hyperthyroid individuals respectively. The study has diagnosed carpel tunnel syndrome in 36 and 17 % of hypothyroid and hyperthyroid individuals. The involvement of nerves in hypothyroidism is due to less active sodium potassium pumps and hyperthyroidism due to hypermetabolism. **Conclusion**: The study has highlighted the involvement of peripheral nerves in thyroid disorders and the role of electrophysiological studies in early detection of neuropathies. The study also suggests to evaluate thyroid function in carpal tunnel syndrome.

Key words: Thyroid disorders, Nerve conduction.

EFFECT OF THYROID DISORDERS ON NERVE CONDUCTION STUDIES IN FEMALES

Introduction:

Thyroid disorders are one of the common endocrine disorders next to diabetes mellitus which has a multi factorial etiology. The prevalence of hypothyroidism in the world population ranges from 1-10% with female predominance and hyperthyroidism affects 2-5% of the women population in the world. In Indian scenario, hypothyroidism is found to affect 1 in 10 adult, and also hyperthyroidism to affect more people. In spite of the fact that India is in post iodination phase, increasing prevalence of thyroid disorders is due to poor awareness and cost factors.

As the thyroid hormone controls the activities of almost all cells in most tissues of the body, altered level of thyroid hormones leads to multi systemic disturbances. Cardiovascular complications like atrial fibrillation and cardiac failure, isolated systolic hypertension, increased appetite and unexplained weight loss are some of the common clinical manifestations of the hyperthyroidism. Poor appetite, weight gain, hypertension, cardiac failure and infertility are some of the common features of hypothyroidism.[1]

In addition to cardiovascular complications, it brings about neurological changes like psychosis, poverty of movements and ataxia in hypothyroid cases and resting tremors and psychosis in hyperthyroid cases. Peripheral neuromuscular involvement in the form of proximal myopathies, entrapment

neuropathies like carpal tunnel syndromes and tarsal tunnel syndromes occurs in both thyroid disorders.

The magnitude of thyroid disorders among poor people of India leads to frequent absenteeism from duty because of the neurological manifestations. Moreover the proper treatment of hyperthyroidism results in complete resolution of neuropathy and late institution of adequate treatment of hypothyroidism does not offer complete cure[2]. Hence it is essential to study the prevalence of the same by doing neurophysiological studies in both symptomatic and asymptomatic patients of established thyroid disorders. And this type of study may necessitate the steps to be taken to increase the awareness among public.

AIMS AND OBJECTIVES

1. To study the pattern of the nerve conduction studies in hypothyroid individuals.
2. To study the changes in nerve conduction pattern in hyperthyroid individuals.
3. To perform nerve conduction study pattern in control groups.
4. To compare the changes in nerve conduction study between hypothyroid and controls.
5. To compare the changes in nerve conduction study between hyperthyroid and controls.
6. To estimate the magnitude of neuropathy in hypothyroid individuals.
7. To estimate the extent of neuropathy in hyperthyroid individuals

REVIEW OF LITERATURE

HISTORICAL ASPECTS

The prescription by Emperor Shen during 2700 BC shows that seaweed can be used for treatment of goiter. This is the earliest evidence related to thyroid gland mentioned in Pen Tsao (1596) which is the herbal of Chinese Pharmacopoeia. In 300 BC, the discussion of goiter is found in Ayurvedic medicine.

In the year 650 AD, use of powdered form of dried mollusc shells and chopped thyroid gland was practiced by a Chinese physician, Sun Ssu-Mo. It was 1500 AD when Leonardo da Vinci first recognized and drew thyroid gland. Andreas Vesalius gave the first anatomical description and illustration about thyroid gland in 1543 AD. Eustachius coined the term Isthmus in 1563 AD. In 1656, the naming of the gland as “thyroid” resembling the shape of an ancient Grecian shield was given by Thomas Wharton[3].

The Latin word “christianus” means the person is not capable of committing a sin. The term “Cretin” was derived from the same and came into use from 1754 AD. Palpitation, goiter and exophthalmos are called as triad of Morbus Flajani. It was named so after the discoverer Giuseppe Flajani in 1802. Bernard Courtois in 1811 AD observed the oxidation of the burnt seaweed with sulfuric acid could give rise to vapor. The vapor was coined as iodine derived from Greek word for violet by Gay-Lussac in 1813 AD. In 1820 Jean Francois

said that the goiter is caused by deficiency of iodine and he used iodine for treating the goiter. It was observation by Alexander von Humboldt during 1825 that the gland size gets reduced when persons suffering from goiter change residence to non endemic area of goiter from endemic area called, Andes. A physician from Brazil, Francisco Freire-Allemao proposed iodine prophylaxis programme. Aqueous solution from Potassium Iodide was proposed by JGA Lugol for treatment of scrofula in 1829.

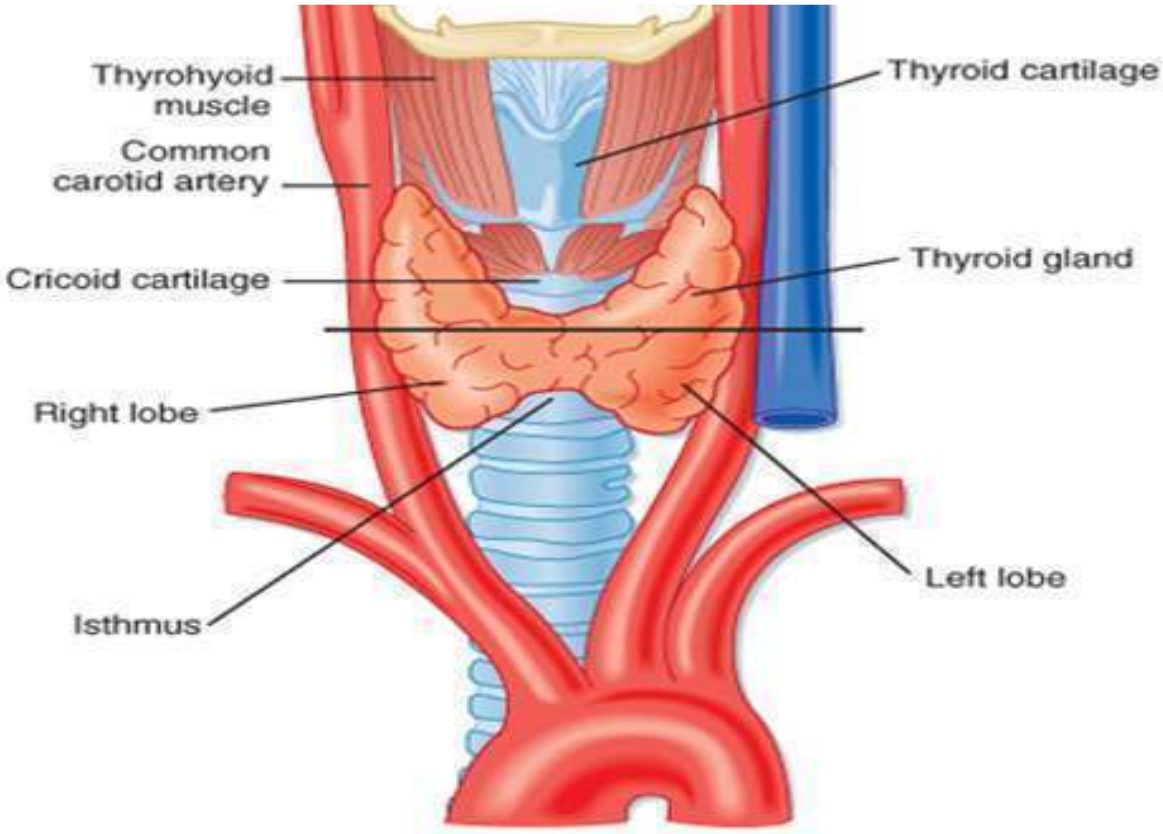
A syndrome consisting of palpitation, goiter and exophthalmos was described by Robert Grave in three women in the year 1834. In individual suffering from cretinism in Switzerland, B.Niepce found out the enlargement of sella turcica in 1857AD. Post operative tetany after total thyroidectomy was observed by Th.Billroth in 1883. E.T. Kocher was the Nobel Prize winner of the year 1909 for his finding of association of myxoedema after thyroidectomy during 1883. He also recommended “half a sheep’s thyroid fried lightly and to take it with a current jelly every week[4].The typical tremor in hyperthyroidism was found out by Pierre Marie in 1888.F.D.Von Recklinghausen reported that osteoporosis can follow hyperthyroidism. The effect of thyroid on basal metabolic rate was reported by Aldolf Magnuu in 1895 AD. The term “iodothyrin” was coined by Eugen Baumann. Pendred found out goiter in deaf mutism in 1897.

Subacute granulomatous thyroiditis was found out by F.de Quervain in 1902.In 1915, thyroxine was isolated by E.C.Kendall and named as thyroxine

by him. Thyroid involution and failure of metamorphosis in hypophysectomised tadpole was described by both Philip E. Smith and Bennet M Allen individually in 1916.Kendall's thyroxine from animal extract of thyroid was introduced in market with high price in U.S.A in 1920. The treatment of Graves' disease using x-rays was proposed by M. Seymour in the same year. Preoperative iodine treatment in Graves' disease was reported by H. S. Plummer in 1924.Nobel prize in 1943 was given to George Harvey for his work on radioactive tracers during year 1924.The chemical structure of thyroxine was discovered by Harington in 1926[5].Harington and Barger revolutioned the treatment of hypothyroidism by synthesizing thyroxine in 1928.Goiter development in cabbage fed rabbits was demonstrated by A. Chesney, T. Clawson and B.Webster in 1930.TSH was extracted and purified from bovine pituitaries in the year 1931.Use of radioactive iodine by Saul Hertz and Arthur Roberts was adopted to study the physiology of thyroid gland and to treat hyperthyroidism between 1937-1943.Negative feedback on pituitary by thyroid was termed as "servo mechanism" by R.G.Hoskins in 1949.In the same year, J . Wolff and I.Chaikoff found out the effect (Wolff Chaikoff's effect) of inorganic iodine on thyroid physiology.

In 1954, triiodothyronine was isolated and synthesized by J.Gross and R.Pitt-Rivers. Genetic abnormality in synthesis of thyroid hormone was identified in the first case by J. B. Stanbury in 1950. Autoantibodies were demonstrated by Roitt and Doniah in 1956 in cases of Hashimoto's thyroiditis.

ANATOMY OF THYROID GLAND

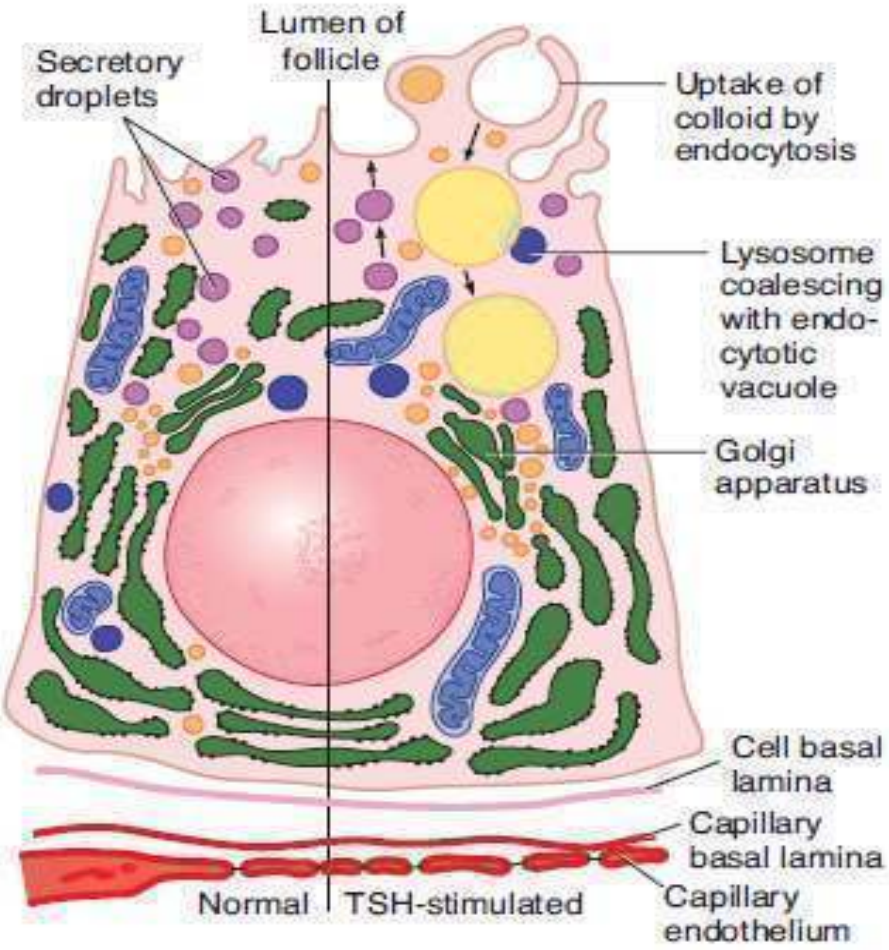


Association of LATS with Graves' disease was discovered by Adams, Purves, and McKenzie in 1960. Demonstration of calcitonin was by D.H.Copp, A.G.F.Davidson, and B.A.Cheney during the year 1963. Breakthrough in estimating hormonal assays by Radioimmunoassay was achieved by S. Berson and R .Yalow in the year 1965.For this contribution they were honoured with Nobel prize during the year 1977.Subsequently L. Braverman S. Ingbar, and Sterling found out the peripheral conversion of T4 to T3, in the same year. A.Schally discovered TRH and he was awarded Nobel Prize for the year 1977. Hetzel in 1971 described the effect of iodine deficiency during pregnancy on fetus nervous system. During year 1972, the receptor for triiodothyronine was found out[6]. Thyroid hormone resistance was demonstrated by S. Refetoff and L. De Groot in 1974. T. H. Liao and J.Pierce were able to obtain ultrapure form of TSH and also found out common alpha subunits in TSH, LH and FSH in 1979.Recombinant TSH was approved in clinical use from 1998. 3-iodothyronine was discovered by Thomas Scanlan in the year 2002.

PHYSIOLOGY OF THYROID GLAND

Thyroid gland, a small bow tie like structure, situated in front of the trachea has got some unique features compared to other endocrine glands. It is the only endocrine gland which is visible and palpable and needs a trace element-iodine for the synthesis of active hormone. This gland synthesizes a hormone which is stored extracellularly as colloid, and stored within the gland as thyroglobulin.

FOLLICULAR CELL IN VARIOUS STATES OF ACTIVITY



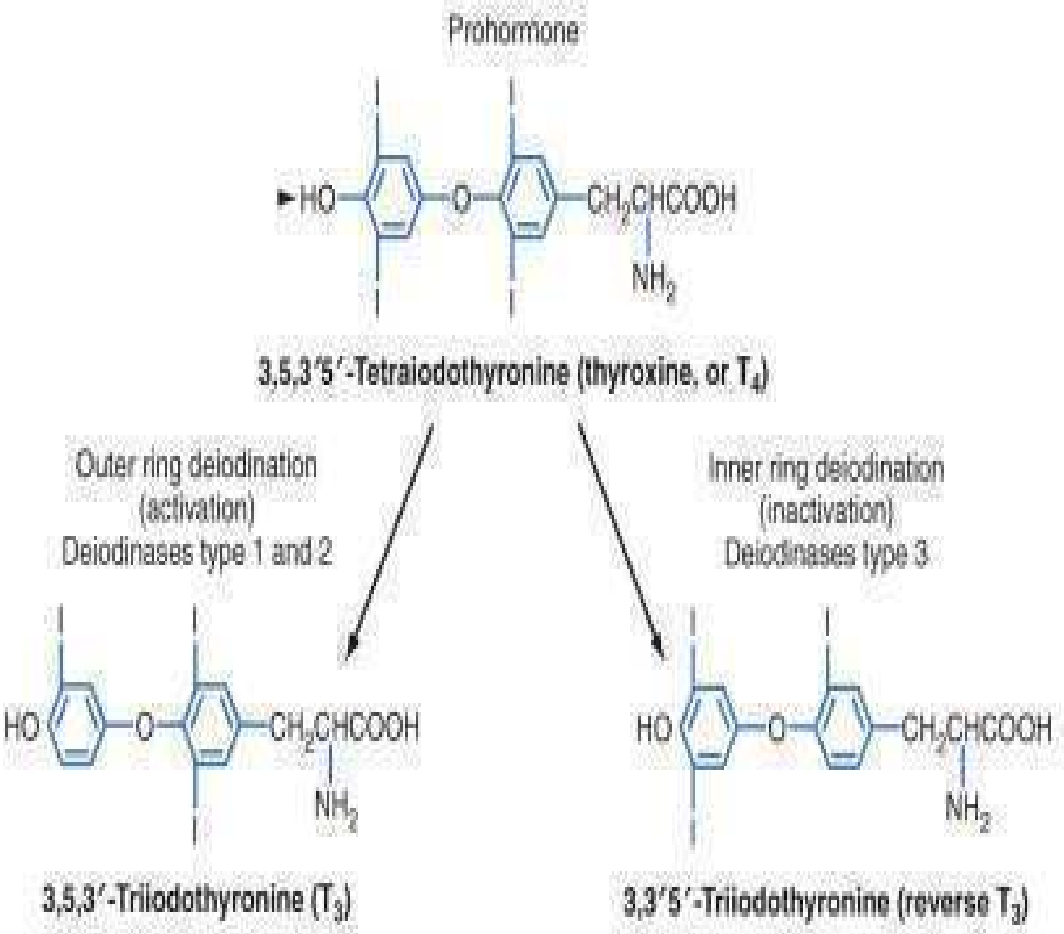
DEVELOPMENTAL ANATOMY:

The thyroid gland develops from the epithelial proliferation in the pharyngeal floor between the tuberculum impar and the copula in the area of foramen cecum and descends down as a bilobed diverticulum. Throughout the period of migration, the thyroid gland is attached to the tongue through thyroglossal duct which disappears subsequently. Failure of disappearance of thyroglossal duct leads to congenital anomaly called as thyroglossal cyst. Up to seventh week of embryonic life, the thyroid gland descends downwards in the midline up to the front part of the trachea.The front of trachea is the postnatal position of the gland. Two lobes and the isthmus in between them develops around ninth week. The first follicle lined by epithelial cells can be seen near the end of third month. This marks the beginning of secretory activity of thyroid gland. The follicle secretes colloid that contains thyroxine and triiodothyronine. Ultimobranchial body gives rise to Parafollicular cells, also called as C cells which secrete calcitonin[7].

FUNCTIONAL ANATOMY OF THYROID GLAND:

The thyroid gland shaped like a butterfly consists of right and left lobes connected by isthmus. The weight of the normal gland is around 20 grams. Histologically , it is formed by many numbers of colloid filled spherical follicles with parafollicular cells in between .The diameter of each follicle measures around 100 to 300 micrometers. Each follicle consists of colloid in its centre surrounded by a single layer of epithelial cells resting on a basement

STRUCTURE OF THYROID HORMONES



membrane. The size of the follicle, amount of the colloid and nature of the epithelial lining depends on the activity of the gland. Inactive gland consists of large sized follicle filled with abundant colloid lined by flat epithelial cells. The active gland has small sized follicles with less amount of colloids lined by either cuboidal or columnar cells with resorption lacunae. The resorption lacunae indicate the active resorption of colloid. Microvilli responsible for formation of resorption lacunae projects from the apex of the epithelial cells into the colloid. Like any glandular epithelial cells, it consists of prominent endoplasmic reticulum and secretory granules. It is the only organ in the body except adrenal cortex receiving blood supply five times more than the weight of the gland[8].

HORMONES SYNTHESISED BY THYROID GLAND:

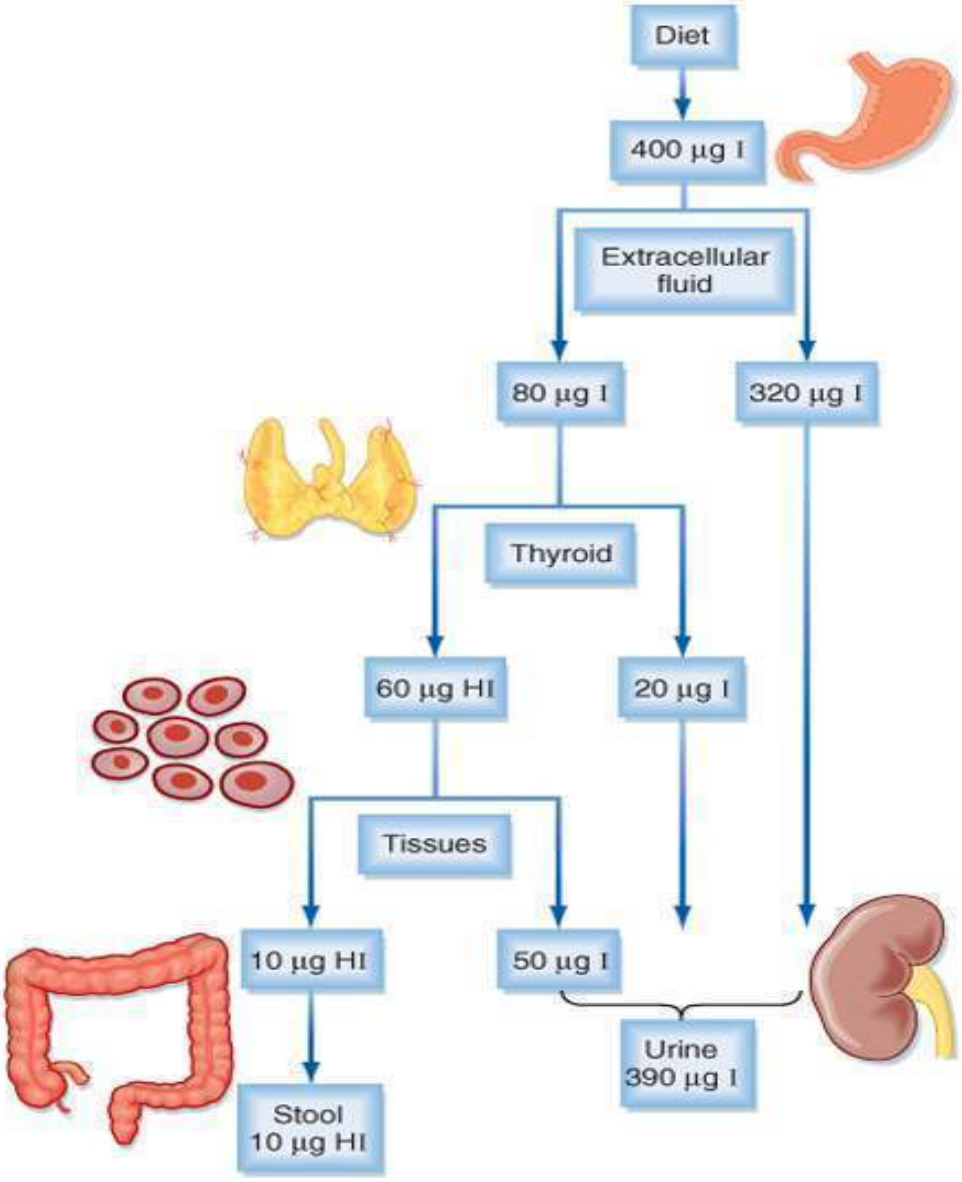
The hormones secreted by thyroid glands are thyroxine or T_4 and triiodothyronine or T_3 involved in basal metabolism and a calcium lowering hormone called calcitonin. Thyoxine and triiodothyronine are synthesized by follicular epithelial cells and calcitonin is secreted by parafollicular cells. T_3 is more potent than T_4. In addition to the above biologically active hormones namely T_4 and T_3, small amount of inactive hormone called as reverse triiodothyronine or rT_3 is also produced by thyroid gland.

IODIDE METABOLISM:

The uniqueness of thyroid hormone is that it needs iodine in trace for its biological activities. The daily requirement of iodine is

Children : 90 to 120 µg

IODINE METABOLISM



Adult	:	150 μg
Pregnant woman	:	200 μg

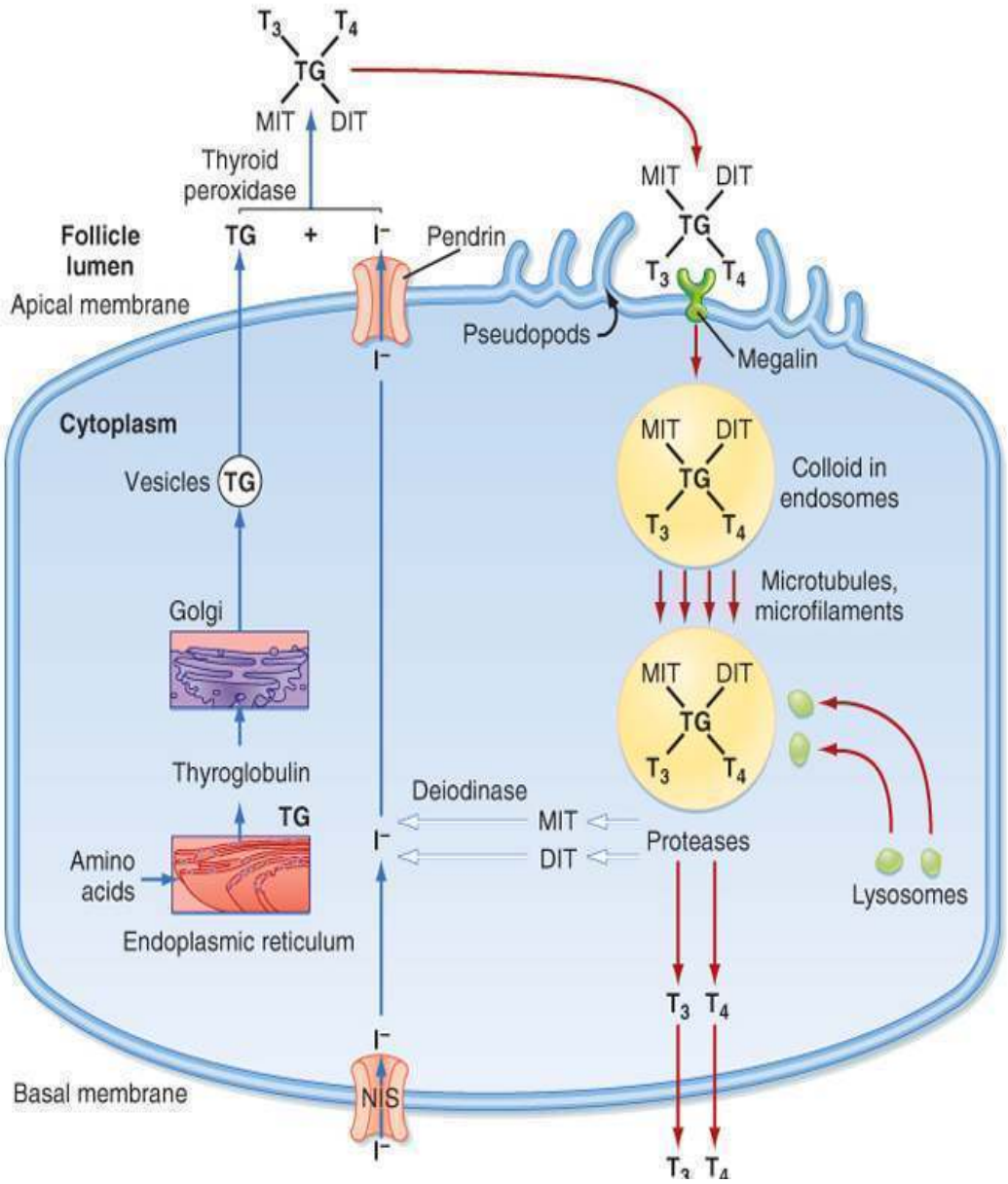
Our daily intake of iodide is around 500 μg which is much more than the minimum requirement of iodide. The food contains this raw material in the form of iodine which in converted to iodide and absorbed in gastrointestinal tract. In the equilibrium state the iodide intake equals iodide excretion. The principle organ taking up most of the circulating iodide is the thyroid gland. In addition, tissues like salivary gland, lacrimal apparatus, gastric gland, mammary glands and choroid plexuses actively concentrate iodide.

The blood contains 250 to 750 μg of iodide. From circulation, thyroid gland extracts 70 to 80 μg of iodide.Thyroid contains around 7500 μg of iodide. The iodide in the thyroid gland is in the form of iodothyronines. Thyroid gland releases around 70-80 μg of iodide i.e. around 1 % of the total iodide in thyroid. Thyroid hormones forms 75 % of the released iodide and remaining 25 % is released as free iodide. As the ratio between the stored iodide in hormonal form and released iodide is more (100:1), human beings are protected from the effect of iodide deficiency for at least 2 months. Kidney also contributes to iodide homeostasis by reducing iodide excretion when there is a fall in serum concentration of iodide[9].

SYNTHESIS OF THYROID HORMONES:

Major hormone secreted by thyroid gland is in the form of thyroxine (93 %). T_3 is formed little (7 %). But most of the thyroxine is converted into

SYNTHESIS OF THYROID HORMONES



triiodothyronine in peripheral tissues by deiodinases. The steps involved in hormone synthesis consists of

- Iodide trapping
- Thyroglobulin synthesis
- Oxidation of the iodide
- Organification of thyroglobulin
- Storage of thyroid hormones.

Precursors like iodide and thyroglobulin involved in thyroid hormone synthesis are moved in basal to apical side of follicular cells. Thyroid hormone after synthesis within the thyroglobulin is moved from apical to basal side for secretion into the blood.

IODIDE TRAPPING:

The iodide entering the circulation from GIT, is actively concentrated into thyroid follicular cells for about 70 times by $2Na^{+}$-$1I^{-}$ symporter (NIS). This transporter is also called as Iodine Pump. This pump brings about influx of two sodium ion by facilitated diffusion and influx of one iodide ion by active transport. The favorable concentration gradient for sodium is maintained by Na^{+}-K^{+} pump .Both pumps are situated in basal aspect of cell membrane.

The activity of iodine pump is modified by altering gene expression. TSH stimulates and iodide inhibits gene expression. Cytokines also inhibits expression. In Iodide deficiency, expression of NIS is increased. Expression of this transporter to a lesser extent is also present in salivary glands, the gastric

epithelium, the placental tissue, the ciliary bodies of the eye, the choroid plexus, the mammary glands, and some cancers derived from these tissues. Drugs like perchlorates and thiocyanates also inhibit the transporter[10].

THYROGLOBULIN SYNTHESIS:

Thyroglobulin containing around 70 tyrosine molecules with molecular weight of 3, 35,000 is synthesized in endoplasmic reticulum of the follicular cell. This thyroglobulin after exocytosed into the lumen of the follicles will undergo changes to synthesize thyroid hormones.

OXIDATION OF THE IODIDE:

Once the iodide is trapped inside the follicular epithelial cells, it is transported into the lumen by a special transporter protein called Pendrin. Deficiency of this protein leads to a disease called as Pendred's disease. Person affected will develop cretinism and sensorineural deafness. After transport, the iodide is oxidised to iodine by the enzyme called Peroxidase. Hydrogen peroxide needed for this reaction is provided by the enzyme called as NADPH oxidase. Both these enzymes are present in the luminal side of the membrane. These peroxidases are inhibited by the antithyroid drugs[11].

ORGANIFICATION AND COUPLING REACTIONS:

Once oxidized, the iodine combines with the tyrosine molecules to form monoiodotyrosine (MIT) and diiodotyrosine (DIT). Coupling of two diiodothyrosine molecules produces thyroxine and coupling of one monoiodotyrosine with one molecule of diiodotyrosine gives rise to

triiodothyronine. This organification and coupling is also catalyzed by peroxidase. Synthesis of T3 is more during iodine deficiency and hyper stimulation of the thyroid gland by TSH[12].

SECRETION OF THE HORMONE:

The thyroid hormone after synthesis is stored in the colloid as a part of thyroglobulin. Megalin, a transporter protein promotes endocytosis of this protein and thyroglobulin is acted upon by lysosomal enzymes. It degrades thyroglobulin into MIT, DIT, T4, T3, rT3 and uniodinated tyrosine molecules. MIT and DIT are broken down into tyrosine and iodine by the microsomal enzymes named intrathyroidal deiodinase[13].

The iodine and amino acids are reused for thyroid hormone synthesis and thyroglobulin synthesis respectively. Because of this recycling process, thyroid hormone deficiency is not manifested up to two months. Deficiency of the deiodinase enzyme can be confirmed by finding MIT and DIT in urine.

TRANSPORT IN PLASMA:

Once secreted into the plasma, 70 % of thyroid hormones bind to Thyroxine binding globulin (TBG) .About 10% to 15 % binds to thyroid binding prealbumin called transthyretin (TTR) .Another 15 % of thyroid hormone is transported as a complex with albumin and 3% by lipoprotein. Among these proteins, albumin due to its large size, possesses largest capacity to bind to hormone as compared to thyroid binding globulin. But thyroid binding globulin has more affinity than albumin. About 0.03% of T4 and 0.3 % of T3

circulates in plasma in unbound form.

Even though thyroid hormone binds to many proteins significant change in the total plasma level of thyroid hormone occurs only when there is a change in the level of thyroid binding globulin. Increase in the TBG level in situations like pregnancy and estrogen therapy leads to increase in the level of total hormones and normal level of free hormones. Drug therapy with glucocorticoids and androgen decreases level of total hormone without altering the free hormone level[8].

The proteins by binding to thyroid hormone act as reservoir for the hormone and also prevent the loss of the hormone by metabolism in tissues or excretion in urine. As the bound form is not filtered at capillary level, it increases half life of the hormone. The unbound form is responsible for hormonal actions. Transthyretin is important for providing the hormones to central nervous system.

TRANSPORT INTO THE CELLS:

Once the hormone reaches the target tissues, it is transported into the cell by specific transporters such as Sodium/taurocholate-cotransporting polypeptides, organic anion-transporting polypeptides, L-type amino acid transporters and the monocarboxylate transporters (MCT). The mutation involving MCT 8 leads to deficiency of intrathyroidal hormone and elevated level of serum T3 and psychomotor retardation. This is called as Allan-Herndon-Dudley syndrome. In this syndrome there is defective transport of T 3 into the neurones during the crucial period of embryonic development.

This leads to decreased myelination[14].

METABOLIC TURNOVER OF THYROID HORMONE:

- About 90 µg of T4, 35 µg of T3 and 35 µg of rT3 are produced daily by thyroidgland.
- Normal levels of total T4, T3 and rT3 are 8µg, 0.12µg and .04µg respectively.
- The levels of freeT4, T3 and rT3 are 2ng/L, 0.28ng/L and 0.2ng/L respectively.
- Half life of T4, T3 and rT3 are 7, 1 and 0.8 days respectively.
- Only 25 % of T3 and 5 % rT3 are formed by thyroid gland.
- Peripheral conversion of T4 contributes to 75 % and 95 % of T3 and rT3 respectively by specific deiodinases.

DEIODINASES:

The three types of deiodinases are D_1, D_2 and D_3. All deiodinases in common contain Selenocysteine, an amino acid containing selenium instead of sulphur. Selenium is important for its enzyme actions. D_1, D_2 converts T_4 to T_3.

- D_1 is present in high amount in liver, pituitary, skeletal muscles, thyroid and kidneys where there is a high blood flow.D_1 regulates the formation of T_3 in peripheral tissues.
- $D_2$is present in high amount in brain tissues and pituitary and brown fat. The high level of deiodinases in brain provides brain tissue and pituitary glands with high level of T_3.

- D_3 is present in brain and reproductive organ converting T_4 to rT_3.Hence D_3 is also called as inactivating enzymes. D_3 is elevated in hyperthyroidism to increase the inactivation of active hormone[15].

FATES OF ACTIVE HORMONES:

T_4 and T_3 after performing the physiological actions, they are either deiodinated into deiodothyrosine or conjugated to their sulfate and glucuronide metabolite. The conjugated metabolites are secreted into the bile. After reaching the intestine they are hydrolysed and reabsorbed partly through enterohepatic circulation and partly excreted into the stool. In addition to the above mechanisms, iodide is also lost into the stool due to the direct entry of hormones from circulation into intestinal lumen. The iodide loss in this route forms 4 % of the total iodide loss[16].

MECHANISM OF ACTION:

Most of the thyroxine hormone once transported inside the cell is converted into T3 and T3 binds to thyroid hormone receptor present in the nucleus.T_4 also can bind to the receptors with less affinity. These receptors form heterodimer with retinoic acid receptors. But this heterodimeric complex does not bind to 9-*cis* retinoic acid though RXR binds to 9-*cis* retinoic acid. They can also form monomers and homodimers. These receptors are kept repressed by corepressor molecules. Once hormones form complex with the receptors,

corepressor molecules attached to the receptors are released and coactivators gets attached. The corepressors[9] are Alien, NCoR and Alien**.** The examples of coactivators are the DRIP-TRAP complex, and SRC family (SRC-1/2/3).These receptor - hormone complex binds to DNA through zinc fingers and bring about the increase in the transcription of genes involved in the proteins. These proteins are either structural or functional proteins. As thyroid receptors binds to specific hormone responsive element of the DNA they can be designated as a member of the superfamily of hormone-sensitive nuclear transcription factors.[17]

THYROID HORMONE RECEPTOR GENES:

There are two types of hormone receptor genes namely THRA,THRB. THRA or TRα genes are present in **chromosome 17** and THRB or TRβ genes are present in **chromosome 3**. Alternative splicing of these genes leads to transcription into two different types of mRNA .These m RNAs gets translated into subcategories of receptors namely $TR\alpha_{1,}$ $TR\alpha_2$, $TR\beta_1$ and $TR\beta_2$.$TR\beta_2$ is exclusive to the brain. There is wide distribution of $TR\alpha_1$, $TR\alpha_2$, and $TR\beta_1$. Among the four types of receptors, $TR\alpha_2$ does not bind to T_3. T_3 has more rapid and potent action than T4 because of its less binding to plasma protein and also its good affinity to TR. RT_3 is inert in binding to the receptors.The mutation of theTR β gene can present as three varieties of clinical problems.

1) Usually the resistance happens both in peripheral tissues and at anterior pituitary level. As TRα is normal and there is high level plasma level of T_3 and T_4, patients do not exhibit hypothyroid state.

But there is an inappropriate increase in the TSH level even though T_3 and T_4 level is high. Exogenous thyroid hormone administration does not suppress TSH level in these individuals.

2) In some patients, this mutation leads to resistance only at pituitary level. This causes a hypermetabolic state and raised plasma T_3 and T4 levels.TSH is normal and at nonsuppressible level.
3) In few patients it can lead to resistance at the level of peripheral tissues and causes hypometabolic state and normal T_4, T_3 and TSH level. These patients need large dose supplementation of hormones to normalise the basal metabolic rate. The role of hTRβ on brain development can be confirmed by a finding that Attention Deficit Hyperactive Disorder (ADHD) is commonly present in individuals with thyroid hormone resistance than its presence in general population[16].

NONGENOMIC ACTIONS OF THYROID HORMONES:

Predominant actions of thyroid hormone take place through genomic influence. In tissues like heart, muscles, adipose tissues and pituitary, it exerts nongenomic actions through the activation of cAMP or signalling cascade mediated by protein kinase. Some examples of nongenomic actions of thyroid hormones are ion channels regulation and oxidative phosporylation .These nongenomic actions take less time than the genomic actions[17].

PHYSIOLOGICAL ACTIONS OF THYROID HORMONES:

Thyroid hormone, by increasing the protein synthesis in almost all tissues of the body, exerts all its physiological actions.

EFFECT ON BASAL METABOLISM OF THE CELLS:

Oxygen is the essential element involved in the oxidative phosporylation reactions in generation of ATP from ADP. The rate of oxygen consumption decides the rate of metabolism in the cells. By increasing the oxygen consumption of the cells, thyroid hormone brings about the increase in the basal metabolic rate. Normally about 250 ml of oxygen is consumed by the body per minute at resting state. In hyperthyroidism it goes upto 400 ml/mt.

The enhanced activity of Na^+- K^+ pump and increase in the mitochondrial enzymes also cause increase in the basal metabolic rate. Enhancement of the metabolism in the cells increases the heat production also. This is known as calorigenic action of the thyroid hormone. Thyroid hormones, by increasing the synthesis of uncoupling of protein 1, increase the generation of heat. Gonads of both sexes, spleen, brain, lymph nodes and uterus are the organs in which the basal metabolism is not altered by this hormone. Thyroid hormone does not bring about the enhancement of oxygen consumption during exercise and after dietary intake[9].

ACTION ON MITOCHONDRIA:

Thyroid hormone increases the size and number of the mitochondria. Also the surface area of mitochondrial membrane is linearly increased with the increase in rate of metabolism. These actions of the hormone increase the production of Adenosine triphosphate (ATP) for increasing the metabolic activity of the cells. But increase in the activity of mitochondria may also be secondary to the increased basal metabolic rate.[18]

ION TRANSPORT:

Activity of the Na^+- K^+ pump is increased by the thyroid hormone. The increased activity of the above pump increases the transport of sodium potassium through cell membrane. The activity of this pump needs ATP. This is the reason for the thyroid hormone to increase the basal metabolic rate. Thyroid hormone also increases the leakiness of sodium channels. The increased activity of the sodium channels in turn increases the activity of the sodium potassium pump and also increases the heat generation.

EFFECT ON GROWTH:

Thyroid hormone promotes growth and maturation.Before the fetal thyroid starts synthesising the hormone around mid gestation, thyroid hormone from mother crosses placenta into the fetal circulation thereby bringing about the growth activity and maturation of fetal organs. Normal nervous system development also requires the thyroid hormones. The bone maturation and formation are also stimulated in fetus by thyroid hormones. This effect on

enhanced growth rate in human being is observed mainly during fetal life and childhood[19].

The children born with the deficiency of thyroid hormone develop cretinism in which the irreversible mental retardation and short stature are the characteristic features. This necessitates the early diagnosis of the hypothyroidism in children. The testing for hypothyroidism in cord blood is nowadays practised in many centres.

The influence of thyroid hormone in growth and maturation is experimentally proved by growing a tadpole of frog in thyroid deficient situation. The effect of this is the arrest of metamorphosis into the frog. In human being the growth rate is increased mainly during childhood

ACTIONS ON CARBOHYDRATE METABOLIM:

It increases the rate of glycolysis, gluconeogenesis by increasing the enzymes involved in the metabolic pathways, absorption of glucose from GIT and increases the secretion and action of insulin[20].

ACTIONS ON FAT METABOLISM:

By increasing the mobilisation of fat stores, thyroid hormone reduces storage of fat. This in turn increases the fatty acid level in plasma and oxidation of fatty acids. By increasing the Low Density Lipoprotein receptors in the liver, it increases the uptake of cholesterol from plasma. This rapid removal leads to increased secretion of cholesterol in bile and then elimination of cholesterol in the stool resulting in reduction in plasma cholesterol level. Thyroid hormone

reduces plasma phospholipids and triglycerides also.

THYROID HORMONES INCREASE VITAMIN REQUIREMENTS:

Most of the enzymes need coenzymes. Essential vitamins act as coenzymes for enzymes. By increasing the activity of enzymes involved in the metabolism, thyroid hormone increases the vitamin requirements. So in case of thyroid hormone excess, there should be adequate supplementation of the vitamins.

ACTIONS ON CARDIOVASCULAR SYSTEM:

As hormone increases the metabolic rate, it results in increased consumption of oxygen and raised metabolic end products. These in turn lead to vasodilatation and increased blood flow in all tissues. Cutaneous vasodilatation leads to the elimination of heat. It also increases the cardiac output, heart rate and cardiac contractility by its permissive actions on catecholamine. Vasodilatation decreases diastolic blood pressure due to reduced peripheral resistance and increased cardiac output increases systolic blood pressure and thus leading to wide pulse pressure. But mean arterial pressure remains unchanged[21].

EFFECT ON OXYGEN CONSUMPTION AND RESPIRATION:

As basal metabolic rate is increased, basal oxygen consumption is also increased. But it will not enhance the increased oxygen consumption met during exercise or after a meal intake. This increased basal oxygen consumption and increased production of metabolic end product results in increase in respiratory

rate and tidal volume. Both effects increase minute ventilation[22].

Thyroid hormone stimulates erythropoietin synthesis. The increased erythropoietin increases the rate of erythropoiesis thereby increasing the oxygen carrying capacity of the blood.

ACTION ON DIGESTIVE TRACTS:

Thyroid hormone increases appetite as intestinal absorption is increased. Intestinal absorption increases in order to increase the availability of substrate for increased basal metabolic rate. Thyroid hormones increase the secretory rate of gastrointestinal digestive juices and motility of the digestive tracts[23].

ACTION ON OTHER ENDOCRINE GLANDS:

There are two mechanism by which thyroid hormone increases the endocrine secretion. By its general action of increase in the basal metabolic rate of all the cells, it increases the secretory activity of the cells of the endocrine glands. Secondly increase in the tissue metabolism increases the requirement of hormones by the tissues.

Increase in the metabolic rate of glucose increases the insulin secretion from pancreas. As bone formation is increased by thyroid hormones, the reduction in blood calcium increases the parathyroid secretion. As steroid hormones which are derived from cholesterol are also inactivated by liver, reduction in adrenocortical hormones by negative feedback increases adrenocorticotrophic hormones (ACTH). The increase in the ACTH in turn increases the adrenocortical output to normalise the steroid hormone level.

ACTION ON REPRODUCTIVE SYSTEM:

It regulates the activity of reproductive system in both sexes. In female it promotes graffian follicle maturation and ovulation. So in female hypothyroidism causes infertility and various menstrual disturbances. In males it enhances spermatogenesis and Sertoli cell differentiation at puberty [24].

ACTION ON NERVOUS SYSTEM:

Thyroid hormone plays a vital role in the maturation and development of nervous system in fetal life and in early part of the childhood. The maximal growth of brain occurs between later half of fetal life and first six months after the birth. In this part of human life, thyroid hormone is required for the initiation and facilitation of the neural cell differentiation and maturation.

It stimulates the growth of both cerebral and cerebellar hemisphere. It also promotes basal ganglia development. Axonal multiplication and branching patterns of dendrites are controlled by thyroid hormone. It also promotes the formation of synapse. Neurotransmitter synthesis is catalysed by enzymes. Thyroid hormone stimulates the enzyme productions. It also enhances the receptors formation for the attachment of neurotransmitters to perform their physiological actions.

Thyroid hormone maintains the optimum amount of the enzyme galactosyl sialyl transferase. This enzyme is very important for myelin formation around neuronal processes. Myelination is an important factor responsible for the faster conduction of impulse. Experiments in animals have proved the facilitatory role

of T4 in generation of nerve growth factors. It is essential for the migration of the neuronal cells during the growth of brain. The velocity and amplitude of stretch reflex is facilitated by thyroid hormones.

Thyroid hormone is important for the higher intellectual functions of the central nervous system. It increases the alertness of the individual and response to all stimuli. Thyroid hormone stimulates the synthesis of enzymes involved in generation of energy for the neuronal cells. In spite of all the above influences, the amount of blood in cerebral circulation is not altered by thyroid hormones. Basal oxygen consumption and glucose metabolism in the nervous system is not changed[25].

REGULATION OF THYROID HORMONE SECRETION:

Thyroid glands are stimulated by thyroid stimulating hormone of anterior pituitary. The thyroid stimulating hormone (TSH) is also called as thyrotropin. Synthesis and secretion of thyrotropin is enhanced by the thyrotropin releasing hormone (TRH) of hypothalamus. By its feedback on anterior pituitary and hypothalamus, the thyroid hormones alter the synthesis and secretion of TRH and TSH.

THYROTROPIN RELEASING HORMONE:

This hormone is produced by the arcuate nucleus and median eminence of the hypothalamus.TRH is also present in other tissues like cerebral cortex, digestive tracts and pancreatic beta cells. This tripeptide hormone has the amino acid sequence of pyro- Glu- His- Pro.The first amino acid is modified to

pyro-Glu. After its release from hypothalamic neurones, TRH is transported by hypothalamic hypophyseal portal vessels.

Once TRH reaches the target cells (thyrotrophs) of the anterior pituitary, it activates the TRH receptors present in the cell membrane. This receptor is a G-Protein coupled receptor acting on Phospholipase-C to release second messengers. The second messengers are diacyl glycerol (DAG) and inositol tri phosphate.DAG activates protein kinase - C. Protein kinase - C upon activation leads to phosporylation of proteins. Inositol triphosphate increases the calcium release from the stores inside the cells. By the above mechanisms, TRH increases the synthesis and secretion of the TSH from pituitary.

The TRH also activates Phospholipase-A_2 leading to release of arachidonic acid from cell membrane. Eicosanoids are synthesised from the arachidonic acid and mediates some of the actions of the TRH.TRH also stimulates lactotrophs to secrete prolactin[26].

THYROID STIMULATING HORMONE:

TSH is a glycoprotein. Its molecular weight is 28-kDa.It is stored in the secretory granules of the thyrotrophs like other protein hormones. It consists of α, β subunits. α subunit resembles the α subunits of follicular stimulating hormone, luteinizing hormone and human chorionic gonadotropin. β subunit is specific for TSH. The receptor for TSH is present on the basolateral side of the follicular cell membrane. TSH receptor is a membrane bound G-protein coupled receptors. Once activated by binding of TSH, the α subunit of G-protein gets

detached from the βγ subunits and stimulates adenylyl cyclase. Adenylyl cyclase produces cAMP which acts as a second messenger. TSH receptor stimulation produces following changes:

- It simulates NIS to increase the iodine uptake and thereby concentrating iodide inside the follicular cells 30 times more than in serum
- Increases the iodination of thyroglobulin
- Promotes the conjugation of the one monoiodo and one diiodothyrosine to form T3 and of two diiodothyrosines to form T4
- Increases endocytosis of thyroglobulin
- Increases lysosomal enzyme activity to cleave the thyroglobulin
- Enhances the secretion of T4 and T3 into systemic circulation
- By its growth factor effect it brings about hyperplasia of thyroid gland[27].

NEGATIVE FEEDBACK EFFECT OF THYROID HORMONES:

Like other endocrine hormones, alternation in the level of thyroid hormones exerts their negative feedback effect through a long feedback loop pathway. It acts on both thyrotrophs and neurons of the hypothalamus. TSH is more sensitive to the changes in the level of free form of thyroid hormone. When level of T4 gets reduced to 50 %, TSH increases 50 to 100 times. The thyrotrophs as a sensor monitor the changes in the T3.The source of T3 for this purpose is met either by the direct entry of T3 from the circulation or deiodination of T4 to T3.TSH level is altered by direct inhibition of synthesis of α and β chains or indirect reduction in the number of TRH receptors on the

thyrotrophs. Genes concerned with the synthesis of α and β chain have an inhibitory T3 response element in the promoter site.

Feedback effect of T3 and T4 is also regulated by somatostatin and dopamine. These chemicals produced by hypothalamic neurons are carried to anterior pituitary through hypophyseal portal system. By altering the set point of thyrotrophs for T3, somatostatin and prolactin increase the sensitivity of thyrotrophs to increased intracellular concentration of T3. Hence the secretion of thyroid stimulating hormone is reduced counterbalancing the effect of Thyrotropin Releasing Hormone. These effects have been demonstrated during the infusion of somatostain and prolactin.

SPECIAL FEATURES OF REGULATION IN FETAL LIFE:

As T3 from mother crosses the placenta and fetal metabolic tissues are immature, increase in the T3 level in the fetus reduces the level of TSH by negative feedback.In immediate postnatal life, rapid metabolisation of T3 and slow recovery of TSH suppression takes place. So if mother is hyperthyroid newborn babies have the risk of developing transient hypothyroidism. The reverse is true in case of babies born to hypothyroid mother.

THYROID FUNCTION TESTS:

It includes

1. Assay of thyroid hormonal levels and measuring TSH level
2. Estimation of binding protein

3. TRH response tests
4. Identification thyroid antibodies
5. Plasma cholesterol measurements
6. Determination of basal metabolic rate[28]

THYROID HORMONES AND TSH ASSAY:

Thyroid hormone and TSH level in serum is estimated by Radioimmunoassay or ELISA methods. TSH measurement is important to differentiate primary thyroid pathology from pituitary pathology.

BINDING PROTEINS ESTIMATION:

It is carried out by resin uptake method. The radiolabeled T3 hormone when added to the plasma binds to thyroid binding globulin in serum. After this, resin is mixed with the plasma in the test tube and free radiolabeled T3 binds to resin. There is an inverse relation between uptake and protein binding site and the hormone level in serum is in direct proportion to resin uptake. If more binding sites are free in TBG as in hypothyroidism the resin uptake is low. In hyperthyroidism due to the reduced number of binding sites in proteins, resin uptake is high.

TRH RESPONSE TEST:

In normal person, TRH administration increases the level of thyroid hormone by increasing the secretion of TSH. In primary hyperthyroidism, uncontrolled negative feedback by excessive T4 produces abnormal TRH response. Same thing happens in pituitary hypofunction. Primary hypothyroidism causes

increased TRH response.

ESTIMATION OF ANTIBODIES:

In autoimmune diseases like Graves' disease and Hashimoto's thyroiditis, specific antibodies are produced. Finding out the level of the antibodies in serum may be necessary for establishing the etiology. These are not practised routinely nowadays.

PLASMA CHOLESTEROL:

The concentration of cholesterol is not measured for routine diagnosis of the thyroid disorders but used as prognostic markers in assessing the effectiveness of treatment of thyroid disorders. There is inverse relation between cholesterol level and serum concentration of thyroid hormone level.

MEASURMENT OF BASAL METABOLIC RATE:

It is increased in hyperthyroidism and decreased in hypothyroidism. This test is not in routine practice for establishment of thyroid pathology.

PHYSIOLOGY OF NERVE CONDUCTION

HISTORICAL ASPECTS:

Invention of cathode ray oscilloscope in 1897 by Braun was the breakthrough in the study of action potentials. In 1903 string galvanometer was found out by Einthoven. Muscle action potential instead of the muscle twitch was recorded in the measurement of conduction velocity in motor nerves by Piper in year 1909 and Munnich in 1916.By stimulating tibial nerve Hoffmann demonstrated the monosynaptic reflex in soleus muscle. It

was named as H reflex in 1918 .To amplify the action potentials, electron tube was made use by Fobers and Thacker in 1920.String galvanometer was used by them to record the action potentials. At Cambridge, United Kingdom, Edger Douglas Adrian recorded action potential in a single nerve fibre by amplifying the signal 5000 times. He observed the similarity of impulses in sensory and motor impulses. He is famous for his contribution of all -or- none law. Cortical representation of pain sensation localised to thalamus was by Adrian. Routine use of acoustic properties of EMG signals in present day clinical practice was also found out by Adrian in addition to his contribution in the development of Electroencephalography. He was honoured with Nobel Prize for his contribution on nerve transmission. In 1922, Joseph Erlanger and Herbert Spencer Gasser, a student of the former found out that difference in conduction velocity of impulse in nerve fibres is directly proportional to the diameter of the nerve fibres. Based on this finding they grouped nerve fibres into three different groups. The large nerve fibres were grouped as type A fibre with maximum velocity and smaller fibres as type C with minimum velocity. In 1944 they received Nobel Prize for the same[29]. John Eccles from Australia devised a micropipette and demonstrated the existence of the potential difference across cell membrane. He demonstrated the ability of the smaller ions in causing greater change in the depolarisation. For this, he studied the effect caused by 32 different ions. Demonstration of ionic mechanism in the event

of postsynaptic inhibition was his yet another contribution. It was year 1929, Denny Brown demonstrated motor unit potential. The publication of the report of action potential in median and ulnar by stimulation was made by Eichler in 1937 for the first time. The modern techniques for measuring conduction in sensory nerves were devised a decade later. By stimulating the motor nerves Harvey and Masland observed the decremental response in myasthenia gravis in 1941. In 1957 Eaton and Lambert used the same procedure in various neuromuscular disorders including myasthenic syndrome. During second world war, the team of Seddon, Alexander GM Waddell of Anatomy department at oxford, Feinstein of Canada and Richard Pattle, an electrical engineer studied the effect of denervation. Pattle volunteered to be the subject for this study. By methods to crush the nerve, they performed hourly electromyography and demonstrated the fibrillation potentials. Larger MUP in neuropathy and smaller MUP in myopathies were the independent observations by Fritz Buchthal in 1941 and Kugelberg in 1945 respectively. Alan Lloyd Hodgkin and Andrew F. Huxley did study on Squid and cattle fish having giant axons because it is easy to introduce many electrodes and measure the resting membrane and action potential[30]. They demonstrated the membrane permeability to sodium and potassium in various phases of action potential and also refractoriness of nerve fibres for about 1 ms. They were the pioneer in devising voltage clamp method. The requirement of energy in the form of ATP for restoration of ions was

demonstrated by them. Huxley independently demonstrated saltatory conduction in myelinated nerve fibres in 1949. He also found out the different bands in skeletal muscle fibre and proposed the sliding filament theory of muscle contraction. In 1963 both Hodgkin and Huxley along with John Eccles were awarded the Nobel Prize. Bernard Katz, while studying the synaptic transmission demonstrated that miniature end plate potential is due to the quantal release of acetyl choline. Role of calcium in releasing neurotransmitters was his yet another finding in synaptic transmission. This work on neuromuscular transmission conferred the Nobel Prize in the year 1970.

Changes in the nerve conduction parameters in peripheral neuropathies were studied by Harvey and Kutfer by doing nerve conduction study. The slowing effect of nerve impulse propagation in ischemia was the observation by Kugelberg in 1944 and Cobb and Marshall in 1954[31]. Conduction velocity was calculated for the first time by Hodes, Laravee and German in 1948.They did it so by stimulating a nerve at its various levels. The electromyography machine was designed by Goldseth in interaction with Jasper and Fizell in 1948. The principle of photographic superimposition in the calculation of nerve conduction velocity in sensory nerve was used by Dawson and Scott in 1949[32]. Dawson by devising digital nerve stimulation technique in 1956 differentiated the sensory potential from antidromic impulse in motor nerve. Simpson during 1956 found out that nerve

conduction is slowed in carpal tunnel syndrome. Use of nerve conduction studies in the differentiation of demyelinating disease and axonal neuropathy was adopted by Lambert and Kaeser. From the year 1960, sensory nerve conduction study was made as an integral part of electro diagnostic study in neurophysiology.

ORGANISATION OF NERVOUS SYSTEM

The nervous system is divided into central nervous system (CNS) and peripheral nervous system (PNS). CNS is formed by brain and spinal cord.PNS consists of nerves arising from or entering into the CNS. The peripheral nerves are cranial nerves and spinal nerves.PNS is subdivided into somatic nervous system and autonomic nervous system. The autonomic nervous system controls the activity of the viscera and this control is purely involuntary.ANS maintains the stability of the internal environment.ANS is again divided into sympathetic (catabolic nervous system) and parasympathetic (anabolic nervous system) components. Somatic nervous system consists of sensory nerve fibres entering into CNS and motor fibres leaving the CNS. The sensory fibres otherwise called as afferent fibre takes information from head and neck, body walls and extremities into the CNS. The motor fibres or efferent fibres leave the CNS to innervate the skeletal muscles[33].

ORGANISATION OF PERIPHERAL NERVOUS SYSTEM:

Group of axons leaving the motor neurons of anterior horn of individual level of the spinal cord forms ventral root and group of axons going through the

dorsal root ganglion to reach the dorsal grey matter of the a spinal level forms dorsal root. Hence ventral root fibers carry motor impulse (efferent) from the spinal cord and dorsal root carries the sensory impulses (afferent) towards the spinal cord. Ventral and dorsal root from a single level of the spinal cord unite to form a mixed spinal nerve carrying both afferent and efferent impulse. Then a mixed spinal nerves divide into ventral and dorsal rami. Dorsal rami innervate the dorsal part of the body and ventral rami innervate ventral part of the body. Vental rami or dorsal rami of one level of spinal cord combine with the corresponding rami of the neighbouring segments to form the various named plexuses. From these plexuses individually named peripheral nerves arise.Cranial nerves arise from or end in their corresponding nuclei.

STRUCTURE OF PERIPHERAL NERVE:

A single nerve on its outer aspect has loose connective tissue sheath called epineurium. Each nerve consists of group of fascicles surrounded by a covering named perineurium. Each fascicle is made up of many axons. Each axon inturn is covered by endoneurium.

The anastamosis of one fascicle with the neighbouring fascicles and shift of axon from one fascicle to another fascicle increase the mechanical strength to a peripheral nerve. The diameter of an individual axons ranges from less than 1 μm to 20 μm. As in peripheral nerves, a special glial cell called Schwann cells forms myelin sheath around the axon. The ratio of unmyelinated axon to myelinated axons is 2:1 in a peripheral nerve[34].

VASCULARITY OF NERVES:

The nerves are supplied by arteries located in the epineurium arranged in longitudinal direction. Throughout the length of the nerve, blood vessels from the adjacent tissues send anastamosing branches to the longitudinally oriented vessels. This is analogous to vascular arrangements in the mesentery of the gut. This preserves the blood supply to the nerve during injuries to the blood vessels. From the epineurium, branches run obliquely to reach the deeper layers of the nerve. The endoneurial capillaries form a tight blood nerve barrier. The blood nerve barrier is impaired in some metabolic neuropathies. If this barrier is broken down in nerve injury, there may be a problem during regeneration. Even though the soma of the neurone supports the axonal metabolism, blood supply to the endoneurium is important to maintain the functions of the axons. The above message is evident from the appearance of clinical features of neuropathy when there is a disruption in the endoneurial blood supply.

STRUCTURE OF NEURON:

The neurons vary in size and shape. But all neurons have three parts namely a cell body, dendrites and an axon. The axon ends at axon terminal which forms neuromuscular junction by giving branches to individual muscle fiber.The relation of nerve fibres to neuron was demonstrated by Augustus Volney Waller. He showed the changes in the neurons after the section of the nerve fibres of frog's glossopharyngeal and hypoglossal nerves[34].

CELL BODY:

Perikaryon and soma are the synonyms for the cell body. Soma is considered as the centre of a neuron. Like any other cells, the cell body is composed of a nucleus and cytoplasm with its organelles. The important cell organelles are Nissl granules, numerous mitochondria and Golgi apparatus and lysosomes. Cytoskeletal proteins are neurofilaments, microtubules and actin filaments. Nissl granules are also known as Nissl bodies. It consists of stacks of rough endoplasmic reticulum.

In nucleus, there is one nucleolus and no centrioles. Some neurons have more than one nucleolus. The presence of nucleolus and absence of centrioles indicate that neurons can synthesize protein but are unable to divide. The plasma membrane is called as plasmalemma[28].

DENDRITES:

They are very short extensions of plamalemma of neurons. Presence of dendrites increases the surface area of the neurons. The dendrites transmit the signals from other cells towards the soma. They also synthesize proteins and generate and conduct action potential in some parts of the brain. A single neuron contains up to 10000 dendrites.

THE AXONS:

A peripheral nerve is a collection of many axons. Axon is also called as axis cylinder. The axon is a long tubular structure which conducts the impulse away from the soma of the neuron. Axoplasm i.e. cytoplasm of the axon

consists of mitochondria, Golgi apparatus and cytoskeletal proteins. The point from where axon originates from the cell body is called as axon hillock. Initial segment, the first portion of the axon, is the continuation of axon hillock. Axon hillock and initial segment in combination are known as axon hillock-initial segment portion. In motor neuron, the initial segment generates the action potential. In sensory neuron the action potential is generated at the first node of Ranvier which is a gap between two Schwann cells enveloping the axons.The Schwann cells form the myelin sheath. Theodor Schwann found the presence of myelin sheaths[33].

Based on myelination, the axons are classified into myelinated and unmyelinated axons. In CNS, myelination is contributed by oligodendrocyte and in peripheral nervous system by Schwann cells. In peripheral nervous system, myelinated nerve fibers are present in large somatic nerves and preganglionic nerve fibers.

MYELIN FORMATION:

The Schwann cell wraps around 1mm length of a nerve fiber about 100 times in double layers. The protein P_0 is an important protein involved in the myelination by connecting extracellular portion of two opposing layers. The mutation of this protein affects the myelination and causes peripheral neuropathies. The gap between the membranes of two Schwann cells is called as Node of Ranvier. At the node of Ranvier, the plasma membranes of nerve fibers are in contact with the extracellular fluid and electrolytes. The length of a node

is around 0.5-1.0μm.The distance between two nodes is 1-2 mm.

Multiple sclerosis is an autoimmune condition affecting motor and sensory nerve fibers causing reduced nerve conduction velocity. In this condition there is a patchy destruction of myelin fibers. Myelination of dorsal column sensory fibers occurs at 4^{th} -5^{th} month of gestation. The myelination of corticospinal tracts starts at 2 months of postnatal life and completed at two years of age. Injury to the nerve fibre leads to the degeneration of axons and myelin but Schwann cells survive and increases in numbers. During the repair of the injured fibres, the Schwann cells forms the myelin sheaths by reinvesting the regenerating axons[35]

ADVANTAGES OF MYELINATION:

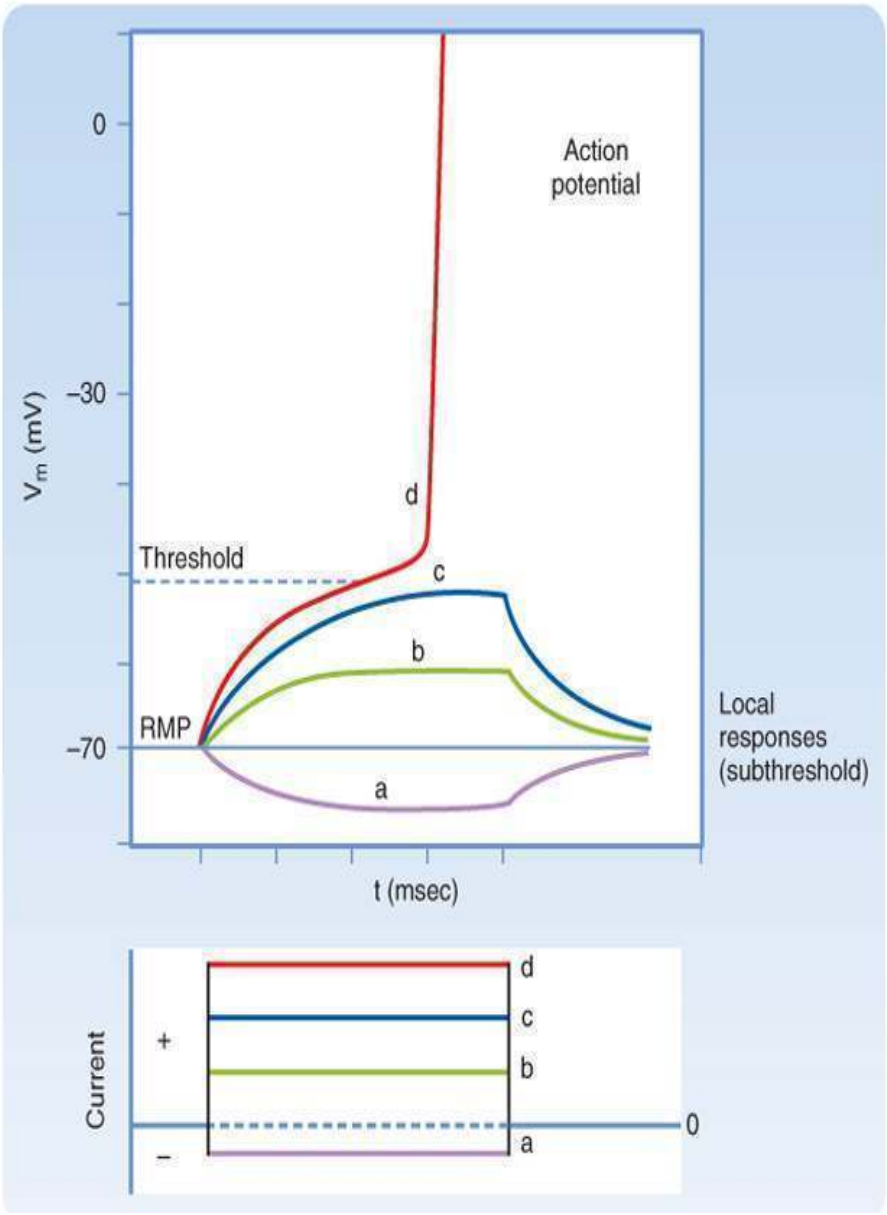
Myelination increases the speed of impulse conduction by a mechanism called as salutatory conduction. It spends less energy for conducting the impulse. In addition it forms a protective covering for the axon.

AXONAL TRANSPORT:

The substances in axoplasm can be transported in either direction of the cell body. Centrifugal transport is also called as anterograde transport and it is either slow in transporting the proteins involved in the growth and regeneration of axon at a rate of 400 mm/day or fast in transporting enzymes involved in the synthesis of neurotransmitter at the rate of 0.5 -2 mm/day. Fast transport is brought about by kinensin.

The centripetal transport is known as retrograde transport. this is usually

SEQUENTIAL CHANGES IN MEMBRANE POTENTIAL



fast at a rate of 200 mm/day. This is carried out by a microtubule associated protein called dynein. This route is used for the transport of nerve growth factors taken up by presynaptic terminal towards soma and for reuptake of neurotransmitters like norepinephrine. The neurotransmitter at presynaptic nerve terminal is either inactivated or repacked into the vesicles. Some vesicles reach the soma through this route to give feedback signal about the need of neurotransmitter synthesis.

Viruses like Varicella zoster and toxins like tetanus toxins also use this route for spread. This is an active transport. The centrifugal transport is mapped by (^{3}H)-leucin and centripetal by horse-radish peroxidase.

The other mode of transport is the transport of nerve growth factor between two neurons at synapse called transneuronal pathway [36].

SEQUENTIAL CHANGES IN THE MEMBRANE POTENTIALS:

At resting state or active state during signal transmission, potential difference exist between both side of the nerve fiber membrane due to the changes in the ionic composition brought about by specific ion channels. This can be recorded either in the form of monophasic response by placing the recording electrode inside the axon and the reference electrode outside the cell membrane or biphasic response by keeping both electrodes extracellularly. The specific ion channels are located on the cell membrane. These may be leaky or gated channels[9].

RESTING MEMBRANE POTENTIAL:

At rest, the cell membrane is at polarized state with a potential of -70 mV inside the cell as compared to outside. This potential is called as resting membrane potential(RMP).This is brought about by presence of nondiffusible anions and leakiness of membrane more to potassium than other ions like sodium and chloride through leaky channels at resting and RMP is maintained by Na^+- K^+ pump[37].

GRADED POTENTIAL:

If a stimulus with less strength is applied, there is a generation of nonpropagated local potential of low magnitude called as Graded potential. The graded potential can be either catelectrotonic (depolarizing) or anelectrotonic potential (hyperpolarizing). Amplitude of the graded potential increases by increasing the strength of the stimulus .If a second stimulus is applied before the disappearance of the potential change produced by the first stimulus, the resultant potential has an increased amplitude. This property of the graded potential is called as summation. Graded potential decreases with time and distance (decremental conduction) Increase in the strength of the stimulus opens up more and more sodium leaky channels. Receptor potential, end plate potential in skeletal muscle and pacemaker potential in smooth and cardiac muscles are examples of graded potential[8].

LOCAL RESPONSE:

When membrane potential is reduced by 7 mV, i.e. from -70 to - 63 mV by a stimulus, with the strength more than for producing graded potential but less than the threshold stimulus, there is a change in the pattern of graded potential called as local response. The amplitude of the potential is larger than the expected for the strength of applied stimulus. It is because of opening of voltage gated sodium channels. In contrast to the graded potential, the local response is always depolarizing in nature. Similar to graded potential, it decreases with the time and distance.

ACTION POTENTIAL:

When a threshold stimulus is applied, it raises the membrane potential to -55 mV. This potential causes instantaneous activation of more voltage gated sodium channels. This potential at which instantaneous activation of sodium channel takes place is called as the threshold potential .The already opened voltage gated sodium opens up further voltage gated sodium channels. This positive feedback mechanism of opening of sodium channel is called as Hodgkin's cycle. Voltage gated sodium channels has the property of fast opening and fast closure. Now the membrane potential changes its polarity from RMP value to the peak through the stages of slow depolarization, threshold potential and rapid depolarization and overshoot. At this period, the membrane is said to be depolarized.

The same stimulus which has opened and closed the sodium channel also

opens the potassium channels which are slow to open and slow to close. Because of the potassium efflux, the membrane potential returns towards the resting state. At this point of time the membrane is said to be repolarized. The repolarizing phase has a rapid falling and a slow terminal phase (after depolarization) [17].

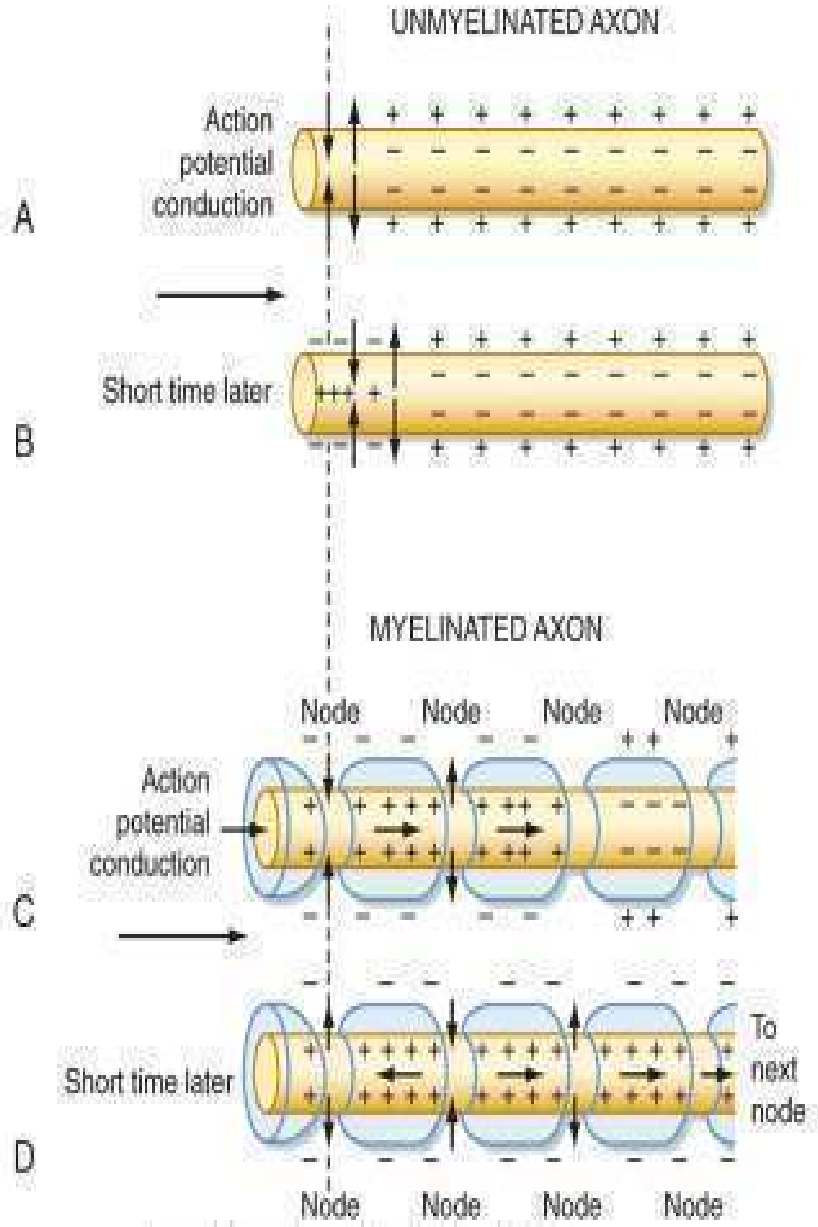
Further efflux of potassium or influx of negative ions changes the membrane potential towards undershoot value than RMP. This state of membrane potential is called as hyperpolarized state. Sodium potassium pump at this time is activated to bring the membrane potential and ionic composition towards the original resting state.

The duration of action potential of a nerve fiber is about 1 msec. The peak value of depolarization is +35 mV.

FEATURES OF THE ACTION POTENTIAL:

1. The action potential once initiated in one part of cell membrane is transmitted from the site of stimulus to other parts of cell membrane of excitable tissues.
2. Once the threshold potential is reached, further activation of the sodium channel takes place irrespective of the initiating stimulus. This is known as autoactivation of the channels.
3. It follows all or none law. Action potential reaches its maximum amplitude to threshold or suprathreshold stimulus or it is not generated at all by subthreshold stimulus.

CONDUCTION OF IMPULSE IN MYELINATED FIBRES AND UNMYELINATED FIBRES



4. Once initiated, second stimulus fails to produce another action potential if is applied within particular duration. This period in which nerve fiber cannot be excited to produce second action potential is called refractory period. This property is important for conducting impulse in only one direction.
5. Unlike graded potential action potential cannot be summated and it is always depolarising[28].

INITIATION AND PROPAGATION OF ACTION POTENTIAL:

The graded potential in the form of synaptic potential is generated at the dendrites or cell bodies of a neuron. The cell bodies of the neurone integrate these synaptic potential and transmits it to the first node of Ranvier of sensory neuron and initial segment -axon hillock part of motor neuron. These regions in the neurones are provided with the higher concentration of voltage gated ionic channels. If this potential is large enough to bring the RMP to firing level, the action potential is initiated. Hence these parts of neuron are termed as trigger zone of the neuron.

Once the action potential is generated at the axon, it is regenerated at regular intervals and transmitted up to the axon terminals. This transmission of action potential is termed as propagation or conduction of impulse which is yet another important property of the action potential.

The diameter and the myelination of the nerve fibres determine the rate and mode of propagation of action potential. The fibers with larger diameter and

myelination conduct the impulse faster. In unmyelinated nerve fibers, after the initiation of action potential at the site of stimulation, circular pattern of current flow regenerates action potential in subsequent segments of the nerve fibre and transmits the impulse.

But in myelinated fibers it is transmitted by a process called saltatory conduction due to the insulating property of the myelin sheath and higher concentration of the ion channels in the nodes of Ranvier. The saltatory conduction transmits impulse faster.

DIRECTION OF TRANSMISSION OF ACTION POTENTIAL:

The action potential is always transmitted in the anterograde direction. That is in motor neuron direction of propagation is from axon hillock to the axon terminal and in sensory neuron it is from the first node of Ranvier towards the central nervous system. This is due to the refractoriness of the depolarised membrane at the site of initiation of action potential. But the action potential can spread in both directions if stimulus is applied in the area between trigger zones and terminal of the axons[37].

PROPERTIES OF NERVE FIBERS:

1. Nerve fibers are excitable
2. They conduct impulse
3. Application of subthreshold stimulus in rapid succession leads to summation and produces an action potential.
4. Nerve fibers follow all or none law and fail to respond to second stimulus

during refractory period.

5. They are unfatigable as conduction of the impulse in nerve fiber does not require much energy.
6. They exhibit the property of accommodation.

CLASSIFICATION OF NERVE FIBRES:

There are two system of classification of nerve fibers. They **are Erlanger and Gasser classification and Numerical classification.**

Erlanger and Gasser classification:

The diameter of the nerve fiber is important factor in determining conduction velocities. This was the explanations for the changes in the shape of the action potential of the nerve when the distance between recording and stimulating electrodes is altered. This was proposed by Gasser and Erlanger. The peak of the compound action potential changes depends on the diameter of the nerve fiber. Depending on the peak, the nerve fibers are classified into A, B, C fibres. Group A fibers are subgrouped into Aα, Aβ, Aγ, and Aδ fibers[16].

The A α nerve fibres with diameter in the range of 12 and 20 μm conducts the impulse at the rate of 70 to 120 m/sec. Sensory fibres carrying proprioception and motor fibers from α motor neurons supplying motor units of the skeletal muscle are examples of A α fibers. A β carrying pressure and touch sensations have the diameter of 5 to 12 μm and conducts action potential at the velocity of 30 to 70 m/sec. The Aγ nerve fibers have thin myelin covering and have the diameter between 3 to 6 μm with the conduction velocities of 15-30m/s.

Motor fibres from gamma motor neurone innervating muscle spindle belongs to this category of the nerve fibers. Sensory fibers conveying pain and cold sensation are of Aδ fibres and diameter is around 2 to 5 μm and conduction velocity in these fibres is 12 -30 m/s. Type A fibers are more susceptible to pressure and less susceptible to local anaesthetic agents.

Type B fibres with diameter less than 3 μm and conduction velocities of 3-15 m/s are present in preganglionic autonomic fiber. Both type A and B fibers are myelinated nerve fibers.

Unmyelinated type C fibers present in dorsal root are small fibers with 0.4 to 1.2 μm and conducts impulses from receptors of pain and temperature at a rate of 0.5 to 1.2 m/s. Type C fibers respond highly to local anaesthetics and less to hypoxia and pressure. Postganglionic sympathetic fibers are also made up of type C fibers. They are made of fibers measuring 0.3 to 1.3 μm in diameter. They conduct impulses at a speed of 0.7 to 1.2 m/s.

NUMERICAL CLASSIFICATION OF SENSORY NERVES:

The sensory nerve fibres are numbered into I a, I b, II, III, IV. Among these groups I a and I b are A α fibers and II and III are made of A β and A δ fibers respectively. Type IV fibres are unmyelinated type C fibers[16].

DETERMINANTS OF CONDUCTION OF NERVE IMPULSES:

As already pointed out, the diameter and the myelination of nerve fiber determine the conduction of impulse.

DIAMETER OF NERVE FIBERS AND CONDUCTION:

Larger nerves conduct impulse faster than the smaller nerves. The diameter of the nerve fibers also decides the internodal length and the degree of myelination. Experiments with computer modelling have proved that the smaller myelinated fibres conduct the action potential faster than larger unmyelinated nerve fibers. The smallest myelinated fiber in mammalian nervous system has a diameter of 2 μm[38].

MYELINATION OF THE AXON:

Myelination by the property of saltatory conduction conducts action potential faster than the unmyelinated fibers. There is a linear relationship between the degree of myelination and the conduction velocity. In case of unmyelinated fibres conduction velocity is directly proportional to square root of diameter of the nerve fibre.

RELATION BETWEEN THE DIAMETER AND MYELIN THICKNESS:

Rushton in 1951, predicted the optimal thickness of myelination from theoretical consideration. The thickness of myelin, in a theoretical model of a fiber with fixed external diameter, is increased at the expense of the internal diameter of the axon and the advantage to conduction velocity by the increased radial resistance is opposed by the increase in axial resistance[39].

Rushton predicted an optimal value of 0.6 for the ‘g’ ratio and later experiments using computer models have confirmed the value for this relationship. But in mammalian fibres it ranges between 0.7 and 0.8 .The higher

value is obtained for nerve fibre with large diameter and lower for the smallest fibres.

$$\text{'g' ratio} = \frac{\text{Diameter of the axon (d)}}{\text{Total nerve fibre diameter (D)}}$$

RELATIONSHIP BETWEEN DIAMETER AND INTERNODAL LENGTH:

There is a linear relationship between diameter and internodal length. The slope of the line of internodal length against diameter changes with growth and elongation of the part of the body. So internodal distance of the median or tibial nerve changes more than that of facial nerve. This linear relationship applies to peripheral nerves but not to the nerve root.

With the advancing age more than 60 years, the sural nerve shows considerable variability in internodal length due to the neuropathic changes taking place because of aging.

NERVE CONDUCTION STUDY

Many neurological disorders manifest clinically in the later part of the disease. Radiological changes also occur after some degree of structural damage takes place. So as to diagnose the disease in early course of the disease, electrodiagnostic studies are performed by using the advances made in the computer technology. These studies help us to plan the treatment in early course of the disease. By starting the treatment in early course of the disease we can

prevent the complications in the form of functional disability. These studies avoid invasive procedures like skin biopsy for quantification of nerve fibers in the epidermis. Action potentials in the form of evoked potential in central nervous system and nerve conduction studies in peripheral nervous system are recorded, displayed, measured and analysed in electrodiagnostic studies by using the equipments installed with user friendly program.

BIOPHYSICS OF ELECTRODIAGNOSTIC STUDIES:

At resting state, excitable tissues have uniformly distributed positive ions outside and negative ions inside the cell membrane. So when two electrodes are kept outside the cell membrane, there is no potential difference between two points of the cell membrane. When the cell is excited by a threshold stimulus, ionic changes by causing differences between two points on the cell membrane permit current flow along the membrane. These potential differences can be recorded as waves. These waves are called as waves of action potentials .It includes[40]

- Compound muscle action potential (CMAP) - motor conduction
- sensory nerve action potentials (SNAP) - sensory conduction
- evoked potentials - CNS

BASIC COMPONENTS OF RECORDING EQUIPMENTS:

Electrodiagnostic equipments consist of both stimulating and recording systems, amplifiers, filters, microprocessor and video and audio monitors in addition to computers.

STIMULATING SYSTEM:

The primary function of a nerve is the transmission of an electrical impulse from one point to another. The stimulus usually comes from the nerve cell body or from sensory receptors.But, in nerve conduction studies the nerve is stimulated by an external electrical source. When the nerve is near the surface of the body, skin electrodes delivers the shock. Deeper nerves require needle electrodes. During surgery, stimulating electrodes are applied directly over the exposed nerves.To obtain a maximal response, all nerve fibres are stimulated by using supramaximal stimulus. Submaximal stimulus gives rise to false results.

RECORDING SYSTEM:

The electrodes are

- Surface electrodes
- Needle electrodes.

There are three types of surface electrodes. They are disc, cup and ring electrodes. Disc electrodes are used in nerve conduction studies and motor evoked potentials and cup electrodes in other evoked potentials. Needle electrodes are employed in electromyography and in some situation in nerve conduction and evoked potential studies. The electrodes are made with various types of metal and alloys. Silver chloride electrodes record noise free stable polarisation potentials.

Three electrodes are used as the components of the recording systems in neurophysiological studies. They are active, reference and ground electrodes.

Motor point in midway between the beginning and ending of the muscles is used for placing the active electrodes in motor conduction study. Reference electrode is placed over the tendons.Between stimulator and the recording electrodes the ground electrode is applied.Both active and reference electrodes are kept over the nerves in sensory nerve conduction studies. Amplitude of CMAP or SNAP is altered if the distance between the active electrode and reference electrode is changed. The recommended interelectrode distance in sensory conduction studies is 4 cms. [41]

PARAMETERS MEASURED IN NERVE CONDUCTION STUDY:

In both motor and sensory conduction studies,

- Latency
- Amplitude
- Duration of CMAP or SNAP
- Conduction velocity

are the parameters used for interpretation of results.

MOTOR CONDUCTION STUDY:

In motor conduction study, nerve is stimulated over two points with suprathreshold strength. Minimum distance of 10 cms is required between two points of stimulation. This distance is changed to shorter segments in the evaluation of entrapment neuropathies like carpal tunnel syndrome. The latency in milliseconds is measured from the point of stimulus artifact to the first negative deflection. Onset latency includes residual latency also. Residual

latency is constituted by neuromuscular transmission time and propagation time along the muscle membrane. For amplitude measurements, either baseline to negative peak or peak to peak is used. The unit of amplitude is the millivolt. Duration is measured between onset to negative peak or onset to positive peak or onset to final return to baseline. The conduction velocity in meter per second is calculated by dividing the distance between two points with the difference between the two latencies. Elimination of residual latency is thus achieved by measuring the difference between the two latencies.

Latency denotes the conduction of the impulse in fast conducting motor fibres and number of intact nerve fibre is indicated by the amplitude. There is a correlation between the density of small fibres and the duration of the amplitude[42].

F Wave:

When motor neurons are stimulated antidromically, it results in conduction of the impulse to and from spinal cord. It happens in between PNS and CNS. It is done by stimulus with supramaximal strength. The cathode is placed proximally and anode distally.

SENSORY CONDUCTION STUDY:

There are two types of sensory conduction measurements. In antidromic conduction study, action potential is recorded over the distal point on the nerve while the stimulation is applied on the proximal point of the nerve. Reverse process is followed in orthodromic conduction. Distal portion is usually a digital

nerve. The surace and ring stimulating electrodes are used for antidromic and orthodromic conduction measurement respectively. Needle electrodes are used in difficult situations.

SNAP is a triphasic form in orthodromic conduction. Triphasic response is due to initial positive peak. This initial positive peak is absent in antidromic conduction studies. Sensory latency is a measurement between the stimulus artifact to the first positive or negative peak. The amplitude of SNAP is either measured between the baseline to negative peak or between negative and positive peaks. Measurement between initial positive peak and the intersection of descending phase to base line gives a measure of duration of SNAP. It can also be measured between the initial positive peak to final return to baseline or between initial positive peak to subsequent positive peak. As no residual latency is present in sensory conduction study, conduction velocity can be obtained by stimulating the nerve at only one point. Distance between the stimulating and recording site divided by latency gives rise to conduction velocity of sensory nerve fibres.

The duration signifies the number of fibres of slow conducting type and the amplitude indicates the density of nerve fibres[43].

FACTORS INFLUENCING CONDUCTION PARAMETERS:

These factors are due to physiological variation or the technical factors involved in conduction study. Age, limb under study and body temperature are the physiological variables affecting the conduction studies .Technical factors

influencing are the stimulating and recording systems of the equipments used and faulty stimulation of the nerve not under study and abnormalities of the nerves.

AGE:

Myelination is not complete at birth. It takes two years for completion of myelination after birth. So in a new born child or infant, the conduction velocity is low as compared to adults. It reaches the normal value of the adult around three to five years of age. Even though degenerative changes in nerves take place in old age, the conduction velocity is not decreased more than 10 meters per second even at eighty years of age. There is a positive correlation between latency of F wave and advancing age [44].

LIMB UNDER STUDY:

Nerves of the upper limbs conduct the nerve impulse faster than the nerves of the lower limb.It applies to both motor and sensory nerves.This is due to the fact that length of the upper limb nerves is shorter than that of lower limb nerves. Temperature of the hands is more than the temperature of feet. Proximal nerve in a limb conducts impulse faster than the distal nerves. This may be due to narrowing of distal axons, reduction in internodal distance. .

TEMPERATURE:

The change in the temperature affects the nerve conduction parameter in both motor and sensory conduction studies. When the temperature is lowered there is a reduction in conduction velocity and increase in amplitude .If the

temperature decreases by one degree Celsius, there is an increase in latency of 0.3 meter per second. Change in the temperature alters the activity of sodium channels. When the temperature is changed from 29 degree celsius to 38 degree Celsius, the conduction velocity is increased by 5 % per degree celsius .

This error can be avoided by performing the study in room temperature 21 to 23^0 celsius. If measured limb temperature is below the 34 degree celsius the warming of limb is to be carried out by immersing the limb in hot water or by using infrared lamps. Otherwise appropriate correction factors are to be adopted while interpreting the conduction parameters[45].

STIMULATING SYSTEMS:

If there is a failure in stimulating system, the submaximal stimulation of nerves takes place. Due to the failure, the applied stimulus fails to travel up to the target part of the study. Both these factors bring about no response in the study or reduced response. The failure may be due to the incorrect placement of stimulators. Sweat or jelly used may influence the conduction. In order to avoid the failure of the system, the stimulating electrodes should be placed closure to the nerve and with the adequate firm pressure. If patient is obese or has edema needle electrodes can be used.

RECORDING SYSTEM:

Incorrect placement of active or reference electrode alters the wave pattern. For example, if active electrode is placed in incorrect position, an initial positive wave is produced instead of initial negative wave. This can also occur

due to the abnormalities of nerve supply or unintentional stimulation of nearby nerves. Hence an investigator should know the anatomical variations of the nerve[46].

INADVERENTLY STIMULATING THE NERVES NOT STUDIED:

The applied stimulus current sometime stimulates the nearby nerve or nerve roots which are not involved under study. This leads to false result in latency variables.

ABNORMALITIES IN THE INNERVATION PATTERN:

Abnormal connection between the nerve produce changes in the amplitude. These abnormal connections may be in the form of connection between the median nerve and ulnar nerve (Martin Gruber anastamosis) .This abnormal connection leads to abnormal nerve supply.

So before starting nerve conduction studies, all the above factors changing the result should be kept in mind to diagnose the nerve conduction abnormality.

PATHOPHYSIOLOGY OF THYROID DISORDERS:

Patients with thyroid disorders commonly seek medical attention for hyperthyroidism or hypothyroidism or goiter. With the availability of sensitive tests for assessing the thyroid function, more numbers of patients are diagnosed to have thyroid disorders.

CLASSIFICATION OF THYROID DISEASE:

Thyroid disease is broadly divided into four categories. They are

1. Excess secretion thyroid hormone
2. Deficient secretion thyroid hormone
3. Resistance to thyroid hormone
4. Neoplasm arising from thyroid gland.

Altered secretion may either be a primary disorder arising from thyroid gland or secondary disorder due to the problem in pituitary gland[47].

HYPERTHYROIDISM:

Pathological condition due to excessive secretion of thyroid hormone in the circulation is called as Hyperthyroidism or thyrotoxicosis. This is named primary thyrotoxicosis due to the pathology in the thyroid gland itself or secondary thyrotoxicosis due to the pituitary disorder. Pituitary disorder causing thyrotoxicosis usually present as TSH secreting tumours.75% of primary hyperthyroidism is due to Grave's disease which is an autoimmune condition followed by multinodular goitre in about 15% of patients. Other causes include toxic adenomas, inflammatory conditions or drug induced. Rarely it is due to extrathyroidal illness like struma ovarii.

CLINICAL PRESENTATION OF HYPERTHYROIDISM:

Patients with hyperthyroidism usually present with weight loss in spite of excessive or normal appetite, inability to tolerate heat, palpitations, tremors and irritable mood. The common signs observed in thyrotoxicosis are tachycardia,

palmar erythema and lid lag. 10 % of patients develop atrial fibrillation responding to beta blockers than to digitalis[48].Goiter is not present in all patients. Experienced physician can easily differentiate uniformly enlarged soft gland of Grave's disease from multinodular enlargement of thyroid gland.

Lid retraction is present in thyrotoxicosis of any cause but ophthalmopathy is present only in Graves' disease. The levator palpebrae superioris muscle is supplied by sympathetic nervous system. As thyroid hormone has permissive action on sympathetic nervous system, lid lag occurs in thyrotoxicosis.

In addition to ophthalmopathy, patient with Graves' disease develop thyrotoxic acropathy and pretibial myxoedema. Patients with thyrotoxicosis have GIT manifestation in the form of diarrhoea reproductive tract anomalies like amenorrhea, infertility and loss of libido. Patients with thyrotoxicosis present with various features of nervous system dysfunction described separately.

THYROID STORM:

It is also termed as thyrotoxic crisis. It is a life threatening emergency. The precipitating factor is usually an intercurrent infection in patients of either asymptomatic thyrotoxicosis or on inadequate treatment. Subtotal thyroidectomy in poorly prepared patients with iodine is also another cause for storm. When a patient develops sudden rise in temperature with confusion or agitations, diagnosis of thyrotoxic crisis should be kept in mind. In addition

patient develops cardiovascular manifestations such as tachycardia or atrial fibrillation and cardiac failure[49].

LABORATORY INVESTIGATIONS:

An elevated or normal T4/T3 in the presence of reduced or undetectable TSH suggests primary thyrotoxicosis. Along with elevated T4/T3 in the presence of elevated TSH confirms secondary thyrotoxicosis. ECG may show sinus tachycardia or atrial fibrillation. For etiological diagnosis, demonstration of antibodies in Graves' disease and radioisotope scanning are done.

SPECIFIC FORM OF THYROTOXICOSIS:

GRAVE'S DISEASE:

This is an autoimmune condition in which autoantibodies produced act on TSH receptors to stimulate synthesis of thyroid hormones and to produce goiter .The antibody is IgG in nature. This is also called as thyroid receptor antibodies or thyroid stimulating immunoglobulin (LATS).It is demonstrable in serum of 80 to 95% of patients with Graves' disease. This condition commonly occurs in women in the age group of 30 to 50 years. This disease is associated with HLA-B8, HLA-DR3 and HLA-DR2. Some patients with Graves' disease do not secrete water soluble form of glycoprotein of ABO antigen. Usually disease onset is preceeded by infection with Escherichia coli and Yersinia enterocolitica. These bacteria have TSH receptors in their cell membrane. So when antibodies are formed against these organisms, they have the property to cross react with the TSH receptors[50].

The patients with Grave's disease develop ophthalmopathy and dermatopathy in the form of pretibial myxoedema in addition to features of thyrotoxicosis. Cytokine induced increase in the number of fibroblasts brings about the synthesis of glycosaminoglycans (GAG). GAG increases interstitial fluid accumulation in the above tissues. The accumulation of fluid is responsible for development of ophthalmopathy and dermatopathy.

HYPERTHYROIDISM IN PREGNANCY:

As pregnancy increases the concentration of thyroid binding proteins, the TSH level tends to change in order to maintain the free thyroid hormone level. So to diagnose the thyrotoxicosis during pregnancy, TSH level should be fully suppressed in the presence of increased level of free hormones. Usually thyrotoxicosis in pregnancy is due to Graves' disease.

As thyroid hormones, thyroid autoantibodies and some antithyroid drugs from the maternal circulation reaches the fetal circulation, fetus is at risk of developing clinical manifestations of hyperthyroidism, drug induced hypothyroidism and enlargement of thyroid gland [51].

HYPOTHYROIDISM:

1 in 100 patients has primary hypothyroidism and about five per 100 patients has subclinical hypothyroidism. Hypothyroidism is more common in females. Hashimoto's thyroiditis and thyroid surgery are the commonest cause for hypothyroidism in areas where there is no iodine deficiency.

CLINICAL FEATURES OF HYPOTHYROIDISM:

The clinical manifestations of hypothyroidism vary with the mode of onset and severity. Degradation of mucopolysaccharides, chondroitin sulphate and hyaluronic acids is enhanced by thyroid hormones. So long standing hypothyroidism leads to infiltration of above substances in various tissues. This infiltration in various organs produces organ specific clinical features of hypothyroidism such as hearing impairment, hoarseness of voice and slurring of speech due to macroglossia. Hypothyroidism forms one of the important causes of carpal tunnel syndrome. Dermal infiltration causes edema of non pitting type. The edema more commonly involves eyelids, hands and feet. Eyelid infiltration gives rise to classical periorbital puffiness of face. There is an increased body weight in spite of reduced appetite. The neurological manifestations are discussed separately. Myxoedema coma is a life threatening complication of hypothyroidism[52].

LABORATORY INVESTIGATIONS:

In primary hypothyroidism T4 level is reduced and TSH level is increased.T3 level is not significantly altered and is not estimated routinely for the diagnosis of hypothyroidism. Raised TSH with T4 and T3 in the low normal level indicates subclinical hypothyroidism. Low T4 and low TSH level indicates secondary hypothyroidism. ECG shows features of low voltage complex with sinus bradyarrythmia. To establish the etiology, investigations like thyroid autoantibodies estimation are to be done.

SPECIFIC FORMS OF HYPOTHYROIDISM:

HASHIMOTO's THYROIDITIS:

It is an autoimmune disorder more common in females. The incidence of this disease in female is 3.5 per thousand per year. In men it is 0.8 per thousand per year. There is a positive association between incidence with the increasing age. It is due to thyroid peroxidase antibodies or thyroid receptor blocking antibodies. Lymphocytic infiltration is the pathognomic of this disease. The goitre is rubbery in nature. The development of lymphoma is a risk associated with the Hashimoto's thyroiditis[53].

IODINE DEFICIENCY:

In Hilly areas like Himalayas, iodine in the diet is low and endemic goitre develops in more than 10 % of the residents of this area. Only very few develop features of hypothyroidism and remainders are euthyroid. Government sponsored Iodination programme has dramatically reduced the incidence of endemic goitre[54].

HYPOTHYROIDISM AND PREGNANCY:

As there is an increased level of thyroid binding globulin and the maternal hormone crosses the placenta during pregnancy, there is a need to increase the dose of thyroxine in hypothyroid pregnant women. Babies born to inadequately treated hypothyroid mother develops cognitive impairment. So repeating thyroid function test every trimester is essential to modify the dose of thyroid supplementation[55].

NEUROLOGICAL FEATURES OF THYROID DISORDERS;

ADULT HYPERTHYROIDISM:

Hyperthyroid patients are anxious, restless and irritable. They are emotionally labile. Their concentrating ability is impaired. They often have headache and insomnia. Older individuals are often depressed and lethargic. This is termed as apathetic hyperthyroidism. Physiological tremors are enhanced and patients have exaggeration of reflexes. New onset of seizure or exacerbation of pre - existing seizure disorders is reported in hyperthyroidism. The seizure related to hyperthyroidism has good prognosis. Abnormal EEG changes revert to normal after the control of hyperthyroidism. Extrapyramidal manifestations like chorea and athetosis are known to occur. Exophthalmos and ophthalmoplegia occurs in Graves' disease. Edema of orbit and lymphocytic infiltration causes proptosis, fullness of the orbital cavity. Extraocular muscle movement are restricted due to edema. Increased activity of sympathetic nervous system causes retraction of eyelids by the effect on Muller's muscle of the upper eyelid. Levator palpebrae's fibrosis is another reason for lid retraction. Optic nerve is rarely infiltrated to cause optic neuropathy. Compression of optic nerve by enlarged extraocular muscles also causes optic atrophy[56].

Goitre may compress recurrent laryngeal nerve and cervical sympathetic nerves and produces vocal cord paralysis and Horner's syndrome respectively.

Neuromuscular involvement in the form of proximal myopathy with fasciculation is common in hyperthyroidism. There is no correlation between the

degree of hyperthyroidism and myopathy. Concentration of creatine kinase in serum is not altered. Myopathy has presented as dysphagia in patient. Myopathy improves once hyperthyroidism is treated[57]. Myasthenia gravis can occur in association with hyperthyroidism. Periodic paralysis occurring in hyperthyroidism resembles hypokalemic type of periodic paralysis. It sometimes occurs in the asymptomatic hyperthyroidism. In contrast to increased incidence of hyperthyroidism in females, this complication occurs more commonly in males. It is usually exacerbated by exercise or intake of high carbohydrate meals. It is more common in Asia. As it resembles hypokalemic type of periodic paralysis, acute attack usually responds to potassium supplementation.To prevent the repeated attack of this complication patient's thyroid status to be normalized. Peripheral nervous system is also involved in hyperthyroidism. It takes the form of sensorimotor polyneuropathy. Peripheral neuropathy in combination with pyramidal tract involvement resembling amyotrophic lateral sclerosis is reported in one case. It has resolved by treatment with radioiodine. When the neuropathy involves lower limb it is termed as Basedow's paraplegia. Goiter does not always coexist with neuropathy in thyrotoxicosis. Hence routine thyroid function test is to be included in the investigations for neuropathy. Confusion and agitation are the neurological features associated with the thyroid storm. It can present as coma also[58].

ADULT HYPOTHYROIDISM:

The most common psychological changes in hypothyroidism are apathy, sleepiness and defective attention. Patient can also have delirium and confusion. This is termed as myxoedema madness. These features disappear with the control of hypothyroidism. Seizures can occur. Hypothyroidism sometimes brings about cerebellar degeneration and manifests as truncal ataxia. Cranial nerve palsy occurs. Asymptomatic cranial neuropathy can be assessed by blink reflex study. Rarely recurrent hypokalemic periodic paralysis has been reported in hypothyroid individuals.

Hypothyroidism very often affects peripheral nervous system and muscles. Proximal myopathy is common.Patients presents with myalgia and muscle stiffness. Muscle enlargement due to edema is termed as Hoffmann's syndrome[59].This can be demonstrated as transient local mounting by percussion. Up to 30.5% of patients presents with carpal tunnel syndrome. In patients with long standing hypothyroidism it may persist even after normalization of thyroid function tests. Sensorymotor neuropathy also occurs. Neuropathy is due to the degeneration of axons and demyelination. Eliciting deep jerks detects slow relaxation of reflexes. Myasthenia gravis occurs in hypothyroidism but more common in hyperthyroidism. If adequate treatment is started earlier the nervous manifestation completely remits. Patients with subclinical hypothyroidism (normal thyroid hormone level with elevated TSH) usually do not exhibit abnormal nerve conduction [60].

Untreated severe hypothyroid patients are at risk of developing myxoedema coma. This presents with features like drastic fall in blood pressure, blood sugar and failure of respiratory movements. If the treatment is not started patient dies.

Hashimoto's thyroiditis is associated with myasthenia gravis. It can induce giant cell arteritis and causes peripheral neuropathy due to ischaemia. Patients having high titre of autoantibody manifest relapsing encephalopathy. The clinical features are confusion, decreased conscious level, myoclonus, tremulousness and seizures. The deterioration resembles stroke. There is diffuse change in electroencephalographic recordings. Cerebrospinal fluid shows increase in protein level with no pleocytosis. Imaging is usually normal except for abnormal uptake in patchy areas.

A study on the rats showed peripheral nervous system is less commonly involved in hypothyroidism than central nervous system. The mechanism of involvement is different in both systems.

HYPOTHYROIDISM IN CHILDREN:

The thyroid hormone plays vital role in the developmental maturation of nervous system. This hormone stimulates growth of the dendrites and migration of neurons. Branching of neuronal process and formation of synapse are under the control of the thyroid hormones. The clinical manifestation of hypothyroidism varies with the age of onset. There are two forms. They are congenital and juvenile acquired hypothyroidism.

Congenital hypothyroidism occurs in one child per 4000 live born children. Babies born with hypothyroidism do not exhibit manifestations of hypothyroidism. This is diagnosed only by screening tests. Screening of hypothyroidism in newborn children is made compulsory in some countries[61]. Commonest congenital form of hypothyroidism is due to maldevelopment of thyroid glands. The gland is either not developed or underdeveloped. In some children it is present as ectopic gland. Female children are more affected than male with the ratio of 2:1. The baby has hoarse cry. Macroglossia and umbilical hernia, prolonged physiological hyperbilirubinaemia are other features. The skin is pale. Both fontanelles are large in size. The baby is lethargic and it is difficult to feed .Constipation is often present. The body movement is reduced. The typical features start appearing after one month of life. The child is hypotonic. The child commonly has sensorineural hearing loss. To prevent the speech and language maldevelopment, this condition is to be recognised at the earliest possible period and treatment has to be initiated. The hearing loss is a constant manifestation of Pendred's syndrome. There is a delay in the psychomotor development. Kocher-Debre Semelaigne syndrome is a type of congenital hypothyroidism in which enlargement of muscles and weakness of movements are present.

The commonest cause of acquired hypothyroidism is Hashimoto's thyroiditis and it can appear at any age of the child. It affects female child commonly.

Endemic cretinism is due to iodine deficiency. The child is mentally

retarded .Malfunctions of corticospinal tracts and extrapyramidal tracts are often present. Deafness developing in this condition usually resolves with early supplementation of iodine.

HYPERTHYROIDISM IN CHILDREN:

Graves' disease is the common cause of hyperthyroidism in children. Rarely hyperthyroidism develops as a congenital condition. Hyperthyroidism is again more common in female children. Male to female ratio is 1:6. Exophthalmos is commonly present. It is present in one or both eyes. The hyperthyroid child is irritable. Attention span is short. There is less concentrating ability. It may sometimes be diagnosed by behavioural problem in school. Deep reflexes are exaggerated. The child has fine tremors. Chorea may be a manifestation. Features of neuromuscular involvement are uncommon. When the child is put on appropriate treatment, the neurological signs disappear [62].

ARTICLES RELATED TO PRESENT STUDY

Unnikrishnan AG et al[63] in a study conducted at 8 major cities in India have observed the rising incidence of all thyroid disorders in India. They also have found that late recognition of congenital hypothyroidism in India due to the poor understanding and nonavailability of screening programmes faces a public health problem even though 1 in 2640 Indian neonates is affected by this disease. Developmental anomalies either structural or functional are the causes of hypothyroidism in childhood. In hypothyroid adult women, they have noticed the common occurrence of the autoimmune etiology as suggested by normal

iodine excretion in urine. 11.4% of females and 6.2% of men are suffering from hypothyroidism. They have suggested a future study on the goitrogenic substance involved in the causation of disease. In this study incidence of subclinical hyperthyroidism is between 0.6 to 1.6 %.

An article by J**uan Bernal**[64] on the influence of thyroid in the developmental maturation of nervous system indicates many unique role of thyroid hormone. It stimulates radial glia to form pathway for the neural cell migration. The formation of a protein called Reelin is enhanced by its gene expression. This protein is essential for the normal organization of layers of cerebral cortex**.**

Wilmar M. Wiarsinga[65] in his article has discussed about the report of the committee held in 1888 narrating the pathophysiological changes in myxedema. He has also enlightened the sequential alteration of the hormones forming the basis for grading the hypothyroidism. Grade I is called as subclinical hypothyroidism where both thyroid hormones are within normal limits and TSH is increased. In grade II, T3 is normal T4 is reduced and TSH is elevated. Grade III is characterised by the altered level of all three hormones.

Song TJ et al[66] in their retrospective study have mentioned that hyperthyroidism can cause seizure disorder. The spectrum of seizure varies from focal to generalised form. Electroencephalographic and clinical manifestations in these patients have subsequently reverted to normal after the definitive treatment.

Pooja Pothiwala et al[67] found that proximal group of muscles are involved in periodic paralysis. It is more common in males. This is diagnosed when potassium level is reduced and the thyroid hormone level is increased. The complete remission can occur only when hyperthyroidism is corrected although acute episodes can be controlled by potassium supplementation.

Out of seven patients diagnosed to suffer from familial periodic paralysis over a period of five years at Mayo's clinic, four patients had hyperthyroidism, says a report by **Harold F. Dunlap et al**[68].

Cesar H Magsino B et al[69] observed that hypokalemic periodic paralysis in some patients is preceeded by the intake of meal containing increased amount of carbohydrate. They also noticed the increased incidence in men than women. Sensory system examination does not reveal any abnormality and patients are mentally normal. Drugs reducing the level of potassium like diuretics can also provoke an attack.

Fisher M et al[70] in their study have found out axonal degenerative changes in one patient with hyperthyroidism. This patient in addition, had involvement of corticospinal tract. It was completely corrected by $\mathbf{I^{131}}$ treatment.

Lai CL et al [71] have demonstrated the normalization of prolonged latencies in the evoked potential studies with the treatment of individuals with hypothyroidism. This highlights the importance of electrodiagnostic studies in hypothyroidism.

Ozata M et al[72] have studied that the changes in the evoked potential

experiments do not return to normal values in both hyper and hypothyroidism even after the normalisation of thyroid functions.

Hala S Sweed et al[73] in their study involving both hyperthyroidism and hypothyroidism have found cognitive impairments. To diagnose the cognitive defect mini mental status examination and P 300 latency were adopted. They also found that significant numbers of patients are suffering from various types of neuropathy as revealed by the changes in the nerve conduction parameters. They have found out sensory neuropathy affects lower limb in 60% of hypothyroid and 75 % of hyperthyroid individuals and it affects upper limb in 80 % of hypothyroid and 75 % of hyperthyroid individuals.

Chiou - Lian Lai et al[74] by doing thyroidectomy in rats performed electrodiagnostic studies to assess the alteration in peripheral and central nervous system. Studies were done before and after supplementing thyroxine. They proved that central nervous system is affected earlier than the peripheral nervous system.

Ihsan M. Azeena et al[75] in a study on patients with thyroid disorders have found out that significant number of individuals suffered from neuropathy and myopathy. The myopathy is of proximal type commonly involving the deltoid muscles. Sural nerve is involved in both groups of patients followed by median nerve. They have also observed carpal tunnel syndrome in notable numbers.

Study by Yeasmin et al[76] have found 67.5% incidence of changes in the

sensory conduction parameter in hypothyroidism. They also divided hypothyroid into two groups one with TSH < 60 m IU and second group with >60 m IU/l and found no significant difference in ulnar nerve sensory conduction parameters between control and first group.

V. Reid et al[77] have found out the recurrence of this syndrome in a hypothyroid patient who has been successfully treated for the same by surgical measures. Study by **Nebuchennykh M et al**[78] showed that mixed fiber polyneuropathy occurs in majority of patients. A follow up study by **El - Salem and Khalid et al**[79] found that it commonly affects deltoid muscles.

Gulbun Yuskel et al[80] in their study on both hyper and hypothyroidism to find out central nervous system involvement and peripheral nervous system involvement have used blink reflex and nerve conduction studies. They have observed significant prolongation of P25 and N20 latency in hypothyroid group and P25 prolongation in hyperthyroid group. They also have observed 54.5 % incidence of carpal tunnel syndrome in hypothyroidism.

Sabina Yeasmin et al[81] have found out a significant significantly prolonged distal latency and reduced conduction velocity in the median, ulnar and common peroneal nerve motor conduction study in hypothyroid group.

Ruurd F Duyff et al[82] have done the nerve conduction study before and after treatment in both groups. They have noticed the early occurrence of sensory nerve abnormalities. The conduction study after treatment has shown the complete resolution of neurological features in all hyperthyroid individuals

and persisting abnormalities in some hypothyroid individual.

SH.Jalil Zadeh et al[83] did a study on 28 patients of subclinical hypothyroid (elevated TSH and normal thyroid hormone levels) group and have observed no significant change in about 25 parameters studied.

Sachin Pawar et al [84] in their literature have pointed out the usefulness of blink reflex study in revealing asymptomatic involvement of cranial nerves in hypothyroid individual. They have found out 50 % of the hypothyroid patients in their study had prolongation of R1 latency.

Ian D Ramsay et al[85] have proved the existence of proximal myopathy in thyrotoxicosis and its complete disappearance after the adequate treatment.[85]

Adikesavan et al[86] in their study on hypothyroid have found sural nerve is most commonly involved nerve followed by median sensory component. Their study did not reveal any significant change in motor conduction parameters of common peroneal and median nerves.

Khedr et al[87] in their study on hypothyroid patients have pointed out that hypothyroidism affected the central nervous system in about 78% of the patients. Peripheral neuropathy was present in 52% of patients. Among peripheral nervous system anomaly entrapment neuropathy affected 35 % of the individual and 9 % of the patient had axonal degeneration type of peripheral neuropathy

Marcia W Cruz et[88] al in the study conducted on 16 hypothyroid individuals have observed the prevalence of 46.6% of myopathy and 43.7 % of carpal tunnel syndrome. None of the patients had polyneuropathy .

MATERIALS AND METHODS

STUDY DESIGN:

Cross sectional study

STUDY CENTRE & PERIOD:

The study was conducted in Tirunelveli Medical College Hospital from May 2014 to Sep 2014.

SAMPLE SIZE:

The study was carried out in 22 hypothyroid, 18 hyperthyroid and 25 normal individuals by case series set up method.

ETHICAL CONSIDERATIONS:

Approval from institutional ethical committee of Tirunelveli Medical College was obtained .The procedure was explained in detail to all subjects in their own local language. Written informed consent was obtained from those persons who were willing to undergo nerve conduction study.

SUBJECT SELECTION:

INCLUSION CRITERIA:

- Newly diagnosed hypothyroid and hyperthyroid individuals attending Tirunelveli Medical College hospital.
- Female patients

EXCLUSION CRITERIA:

- Diabetic and hypertensive patients
- Patients with preexisting neurological disorders

- Pregnant women
- Smoking and alcohol intake
- Use of drugs causing neuropathy
- Liver and kidney disease
- Family history of neuropathy

PROCEDURE:

CLINICAL EXAMINATION:

Those patients willing for study were enquired about the presence of the illness or drug intake mentioned in the exclusion criteria. The patients were clinically examined to rule out hypertension and to find out the sequelae of the past neurological or rheumatological illness. Diabetes and liver and kidney diseases were ruled out by relevant biochemical investigations.

NERVE CONDUCTION STUDY:

The study subjects were explained about the procedures. The sensory nerve conduction study was performed in left median and left ulnar nerves of upper limb and left sural nerve of lower limb. The nerves examined for the motor nerve conduction study were median and ulnar nerves and posterior tibial nerve of the left side.

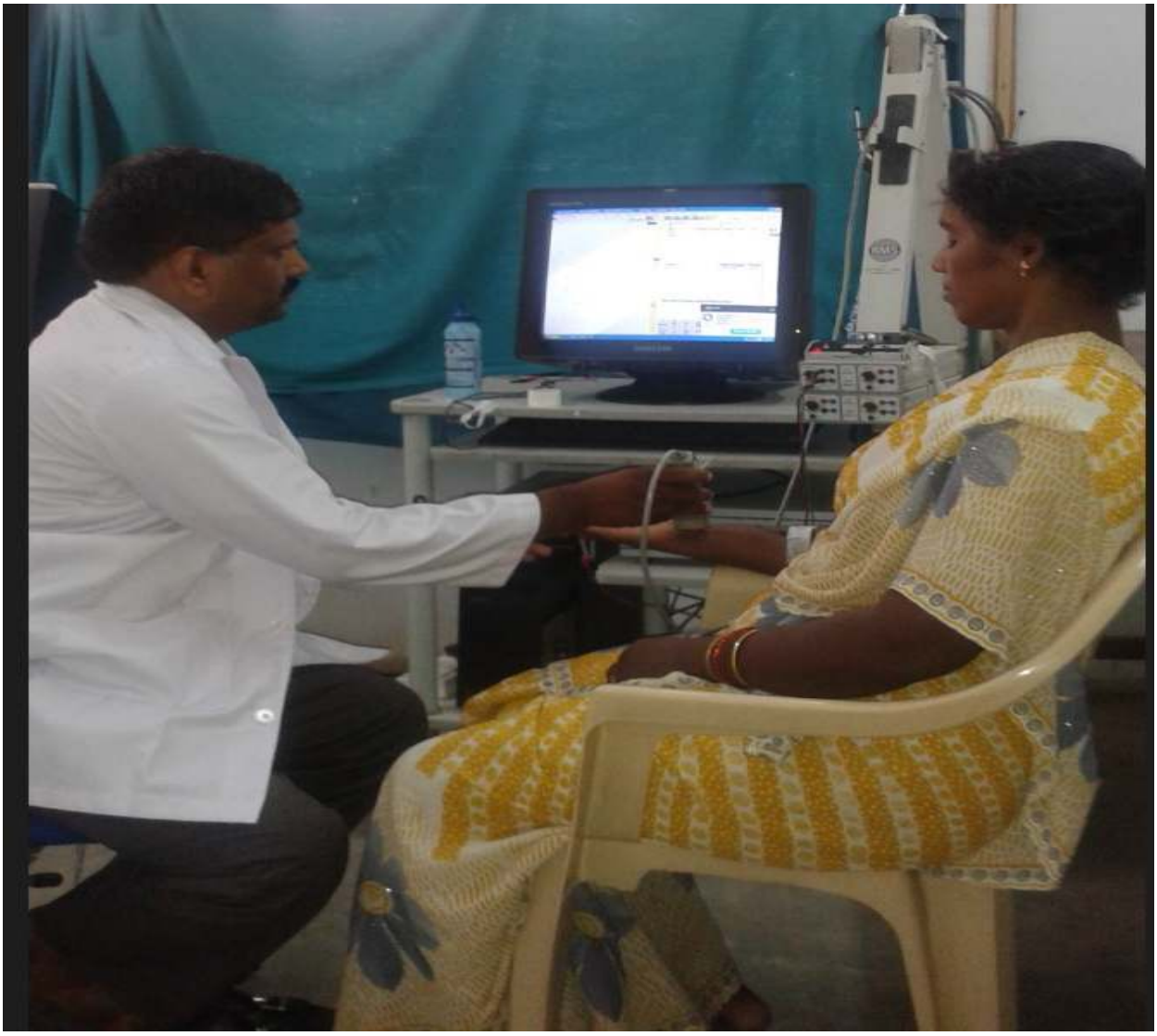
EQUIPMENT USED :

The nerve conduction study was performed by using **RMS EMG EP MARK II** at Neurophysiology unit of the neurology department. Surface electrodes were used. This equipment used filter frequency of 2 to 10 Hz in motor

HYPOTHYROID PATIENT WITH GOITER

HYPERTHYROID PATIENT WITH GOITER

NERVE CONDUCTION STUDY



conduction and 2 to 3 Hz in sensory conduction studies. Initially nerves were stimulated with low voltage strength of current and gradually increased till we obtained a maximal response curve.

PREPARATION:

The skin was cleaned with the spirit and allowed to dry. Skin preparation is essential to provide a good contact between the skin and the electrodes and to eliminate artifacts. The electrodes used were soaked in normal saline to minimise skin resistance thereby facilitating conduction. Adequate electrode gel should be applied to the recording electrodes used in motor conduction study while fixing it to the skin. Correct placement of electrodes is also important.

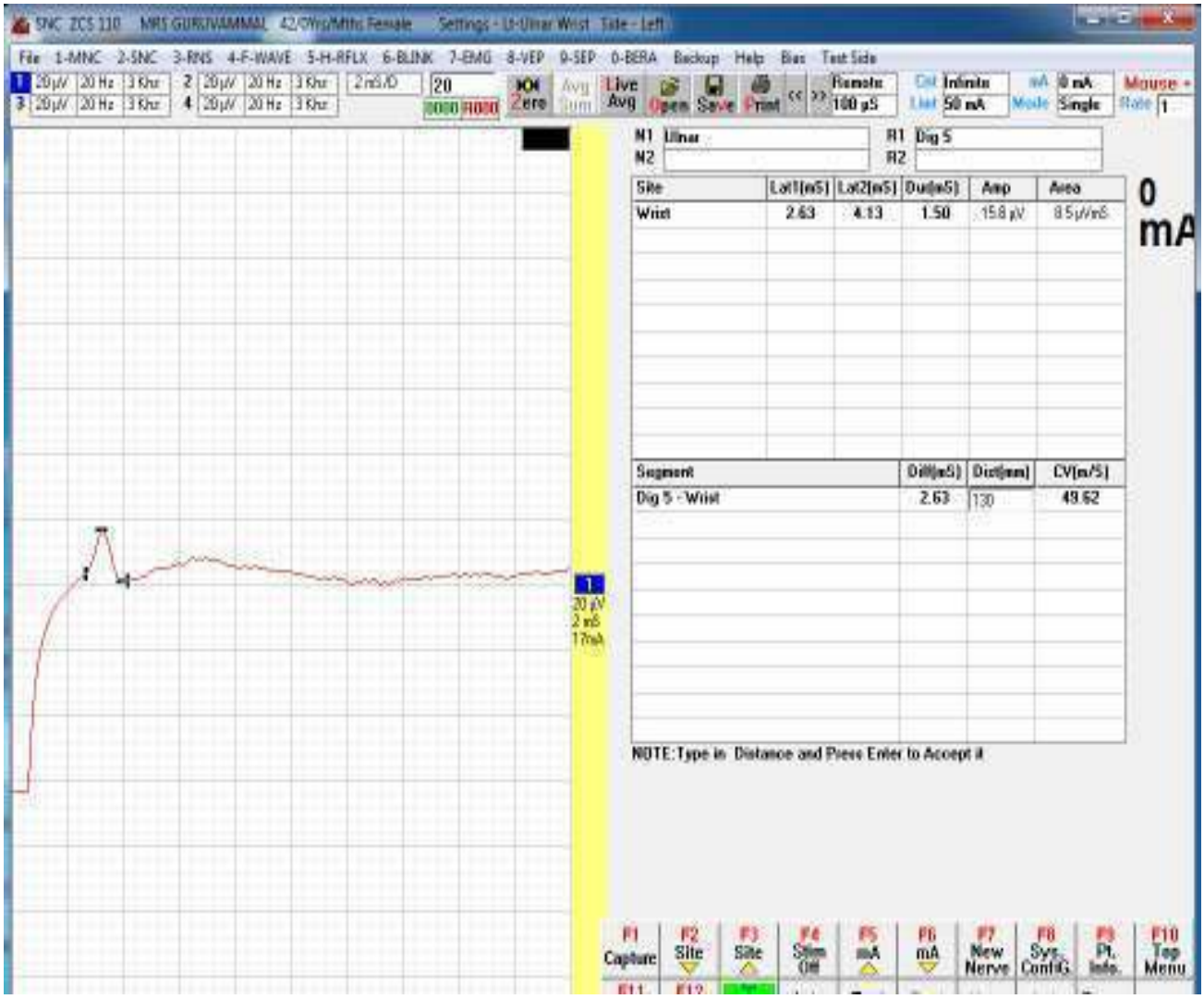
SENSORY CONDUCTION STUDY:

The electrodes were attached to their respective site after preparation of both skin and electrodes and the nerves were stimulated at a single site .The recording electrodes were ring electrodes. The antidromic sensory conduction study was done.

MEDIAN NERVE:

1) The site of placement of active electrode was proximal interphalangeal joint of the second finger.
2) The reference electrode was placed on the distal phalanx of the same finger.
3) The ground electrode was over the dorsum of the hand.
4) Nerve stimulation was carried out at the wrist between the palmaris longus and flexor carpi radialis tendons, at the second distal most crease.

SENSORY CONDUCTION TRACING



5) Peak latency of less than 3.1 ms and minimum conduction velocity and amplitude of 50 m/sec and 20 μv respectively were taken as normal parameters.

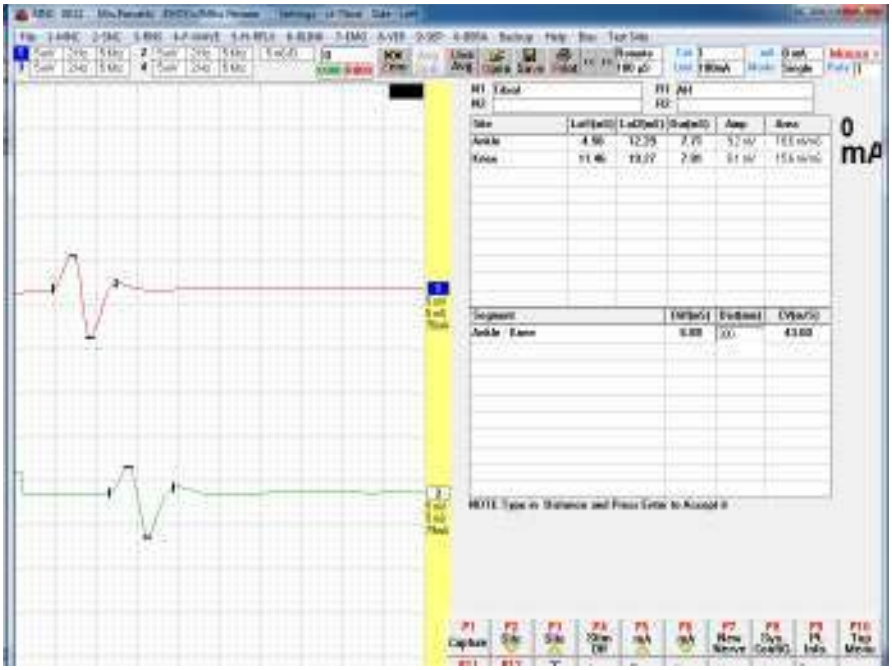
ULNAR NERVE:

1. Active electrode was placed around the proximal interphalangeal joint of the 5th finger.
2. Reference electrodes were placed at the distal Phalanx of the 5th finger.
3. Ground electrode was attached to the dorsum of the hand.
4. Study was performed by stimulating the nerve at the wrist medial to the flexor carpi ulnaris tendon, at the second distal most crease.
5. Normal parameters included maximum latency of 3.5 ms and minimum conduction velocity of 50 m/sec and amplitude of 17 μv.

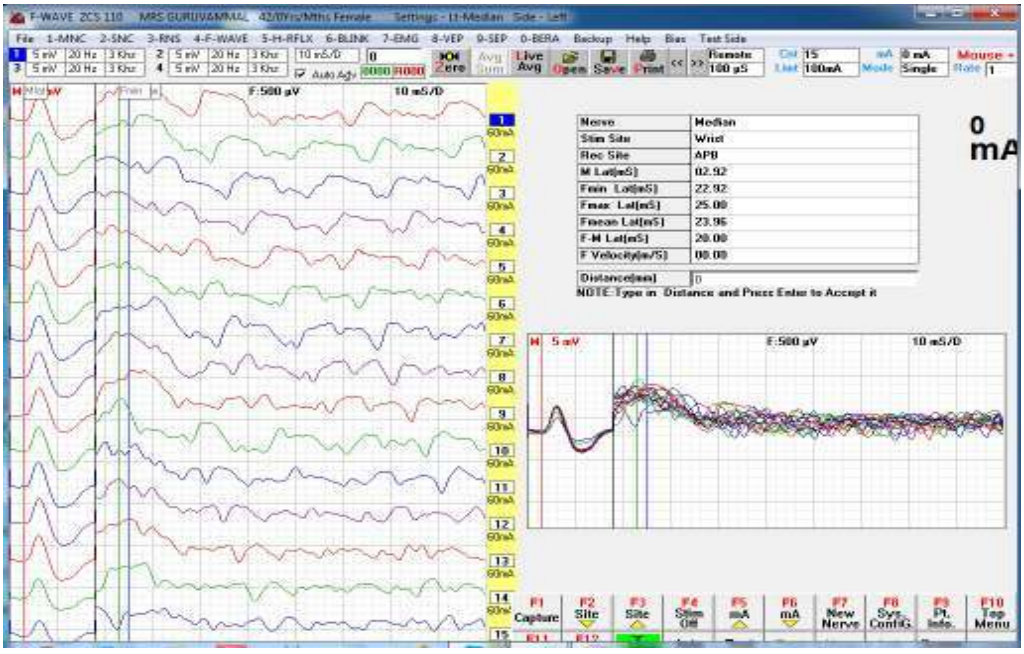
SURAL NERVE:

1) Active electrode was placed between the lateral malleolus and the achilles tendon at the malleolar level
2) The reference electrode was placed 3 cm distal to the active electrode.
3) Nerve stimulation was done at a point distal to the lower border of the bellies of the gastrocnemius 10 to 16 cm above the lateral malleolus just lateral to the midline.
4) We used maximum latency of 4.2 s and minimum conduction velocity of 41m/sec and minimum amplitude of 6 μv as normal values.

MOTOR CONDUCTION GRAPH



F WAVE TRACING



MOTOR CONDUCTION STUDY:

After adequate preparation, the recording electrodes were attached to the correct position with reference to the nerve to be studied. The nerves were stimulated in two points. The distance between the two points of stimulation was measured and entered for calculation of conduction velocity.

MEDIAN NERVE:

1. Active electrode was placed over Abductor pollicis brevis
2. Reference electrodes were placed over the tendon of the muscle
3. Ground electrode was placed over the dorsum of the hand
4. Nerve was distally stimulated at the wrist between the palmaris longus and flexor carpi radialis tendons at the second crease.
5. For proximal stimulation of nerve, the stimulator was placed at the elbow crease, medial to the biceps tendon and brachial artery.
6. Normal values are maximum onset latency of 4.4 ms and minimum conduction velocity and amplitude of 49m/s and 4 mV respectively.

ULNAR NERVE:

1) Active and reference electrodes were placed at the belly of the abductor digiti V and the lateral aspect of the 5th metacarpophalangeal joint respectively.
2) Dorsum of the hand was the site of attachment for ground electrodes.
3) Nerve was stimulated distally at the wrist (just medial to the flexor carpi ulnaris tendon) and proximally at the elbow slightly above the ulnar groove

4) Maximum latency of 3.3 ms and minimum conduction velocity and amplitude of 49 m/sec and 6 mV were taken as normal values.

TIBIAL NERVE:

1. Active electrode was placed over the abductor hallucis, slightly below and anterior to the navicular tuberosity and the reference electrode was placed distally near the metatarsal head.
2. Ground was placed between distal stimulation site and the recording electrode.
3. The distal site of stimulation was behind and proximal to the medial malleolus and the proximal stimulation being the popliteal fossa, along the flexor crease of the knee slightly lateral to the midline of the popliteal fossa.
4. We took the maximum latency of 6.1 ms and minimum conduction velocity and amplitude of 41 m/sec and 3 mV respectively as normal values.

F wave latency was recorded by stimulating the nerves at the distal point to get 10 to 20 F waves.

RESULT ANALYSIS:

After performing the conduction study, the latency, conduction velocity and amplitude of the action potential of both motor and sensory conduction were entered in master chart and tabulated. The statistical analysis was done using unpaired student ‘t’ test and the statistical significance between the groups was obtained.

TABLE 1 AGE GROUP OF THE SUBJECTS

S.No..	Age Group in years	Hypothyroid n = 22	Hyperthyroid n = 18	Control n = 25
1	21-30	8	6	7
2	31-40	7	6	9
3	41-50	7	6	9
4	Mean age	34.68	34.72	36.52
5	SD	8.752	8.75	8.10
6	'P' value	0.46	0.49	-

***P value >0.05 not significant SD =standard deviation**

The study group consisted of 25 normal, 22 hypothyroid and 18 hyperthyroid individuals. The mean age of the various groups under study showed no significant difference when statistically compared.

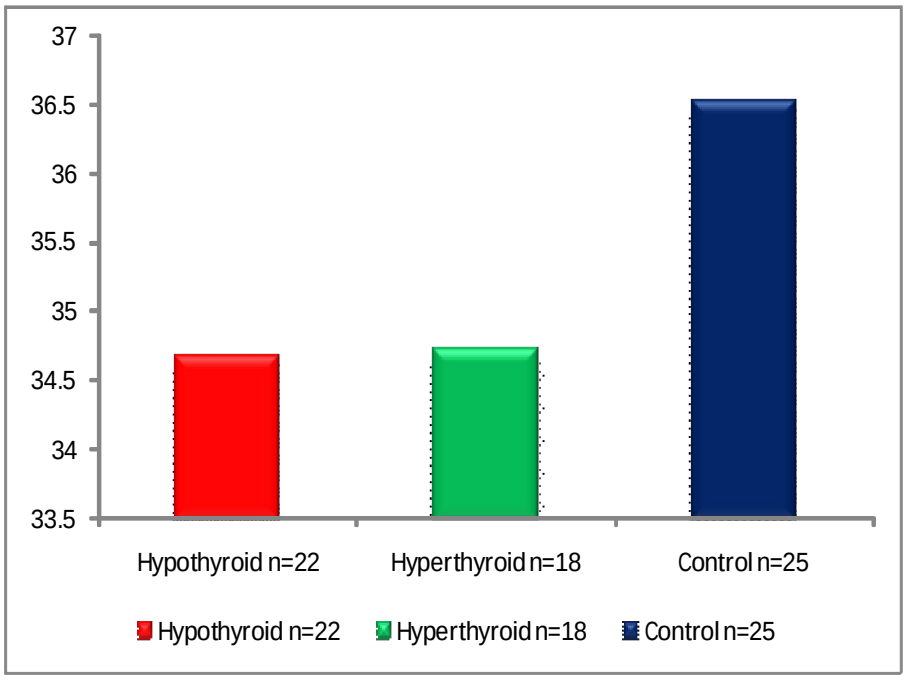
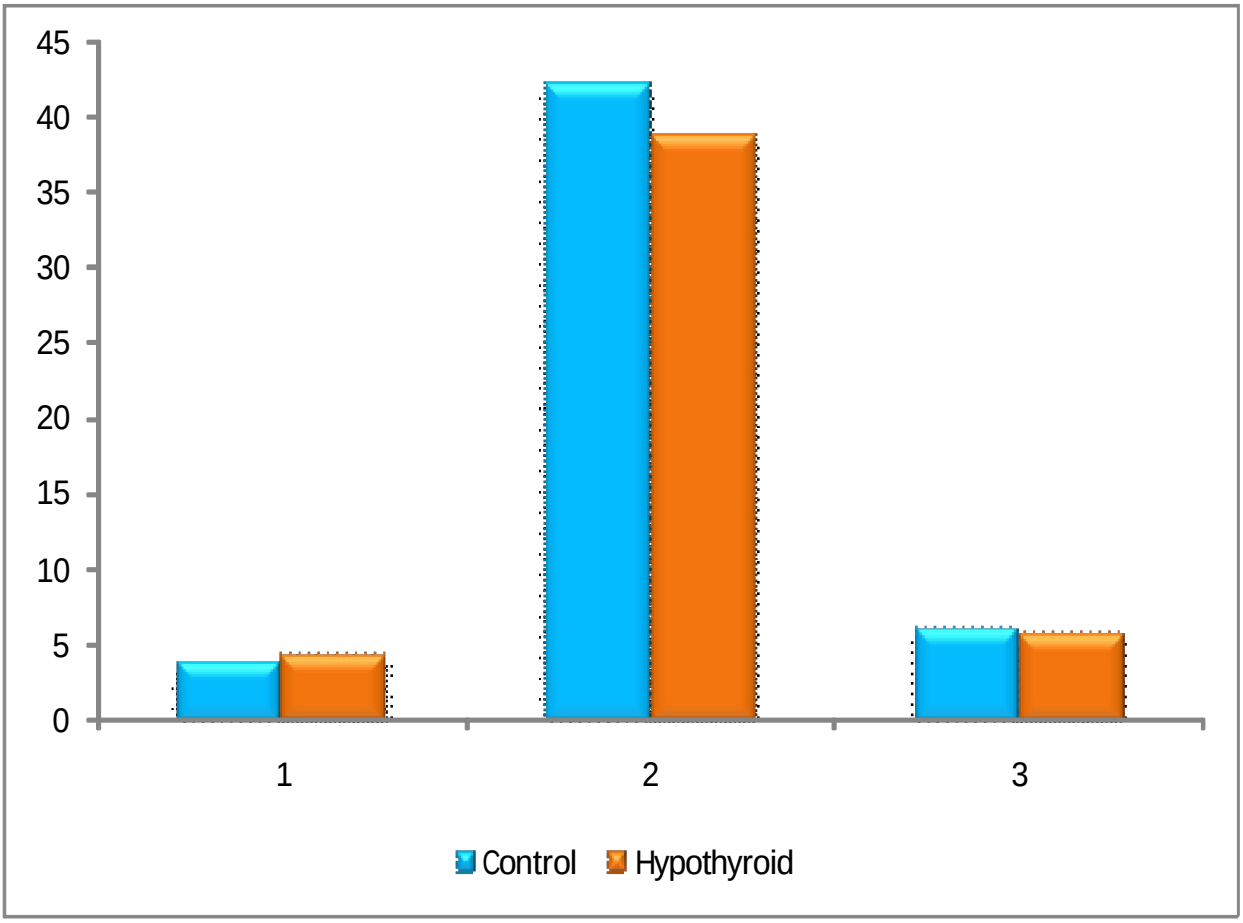


TABLE 2: SENSORY CONDUCTION OF SURAL NERVE

Parameters	Control	Hypothyroid	'P' value
Latency(ms)	3.97 ± 0.26	4.51 ± 0 .61	.001*
Conduction velocity (ms)	42.20±1.86	38.84±5.01	.006*
SNAP(µv)	6.2 0± 0.41	5.75 ± 0.51	.002*

* **P value <0.05 significant**

The sensory conduction study of the sural nerve showed that there was a significant increase in the latency and decrease in the conduction velocity and amplitude of sensory action potential in hypothyroid group.



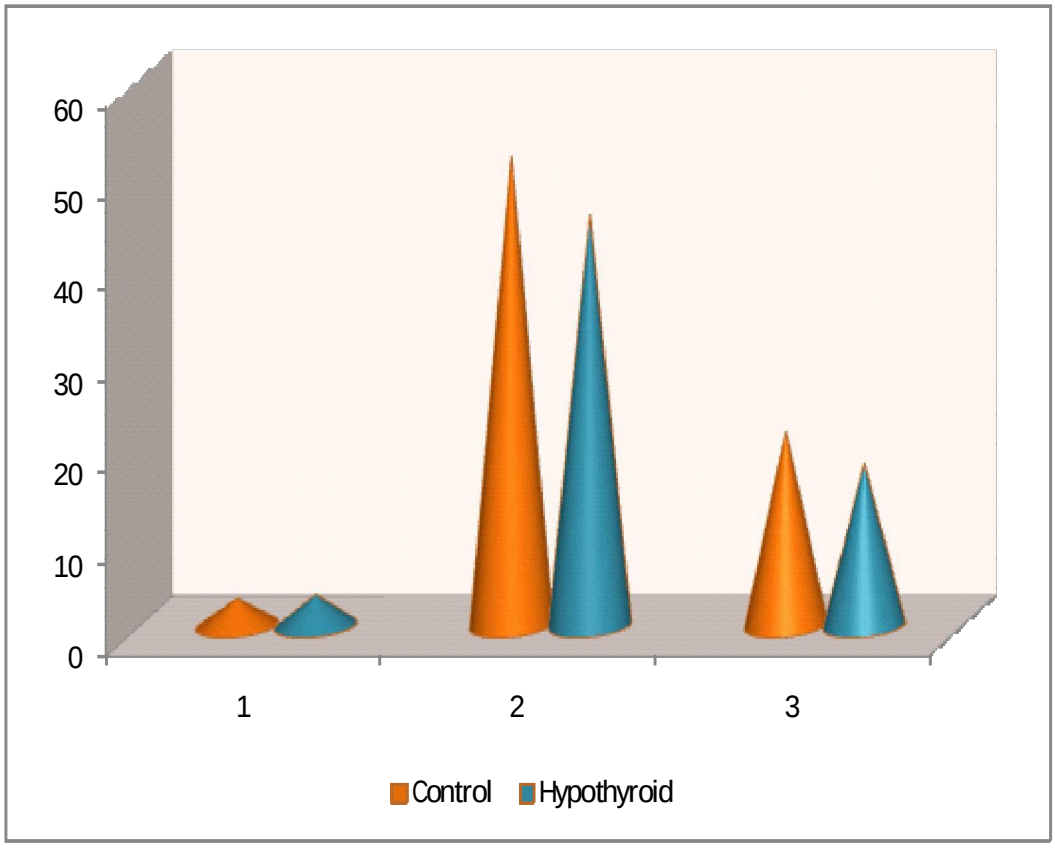
1-Latency 2-Conduction velocity 3.SNAP

TABLE 3: SENSORY CONUCTION OF MEDIAN NERVE

Parameters	Control	Hypothyroid	'P'value
Latency(ms)	2.99 ± 0.19	3.45 ± 0.41	0.000*
Conduction velocity (m/s)	51.42 ±1.56	45.01 ± 8.04	0.001*
SNAP(µv)	21.35 ±1.39	17.80 ± 3.28	0.000*

***P value <0.05 significant**

The statistical analysis of sensory conduction parameter showed a significant increase in the latency and decrease in the conduction velocity and amplitude in hypothyroid group.



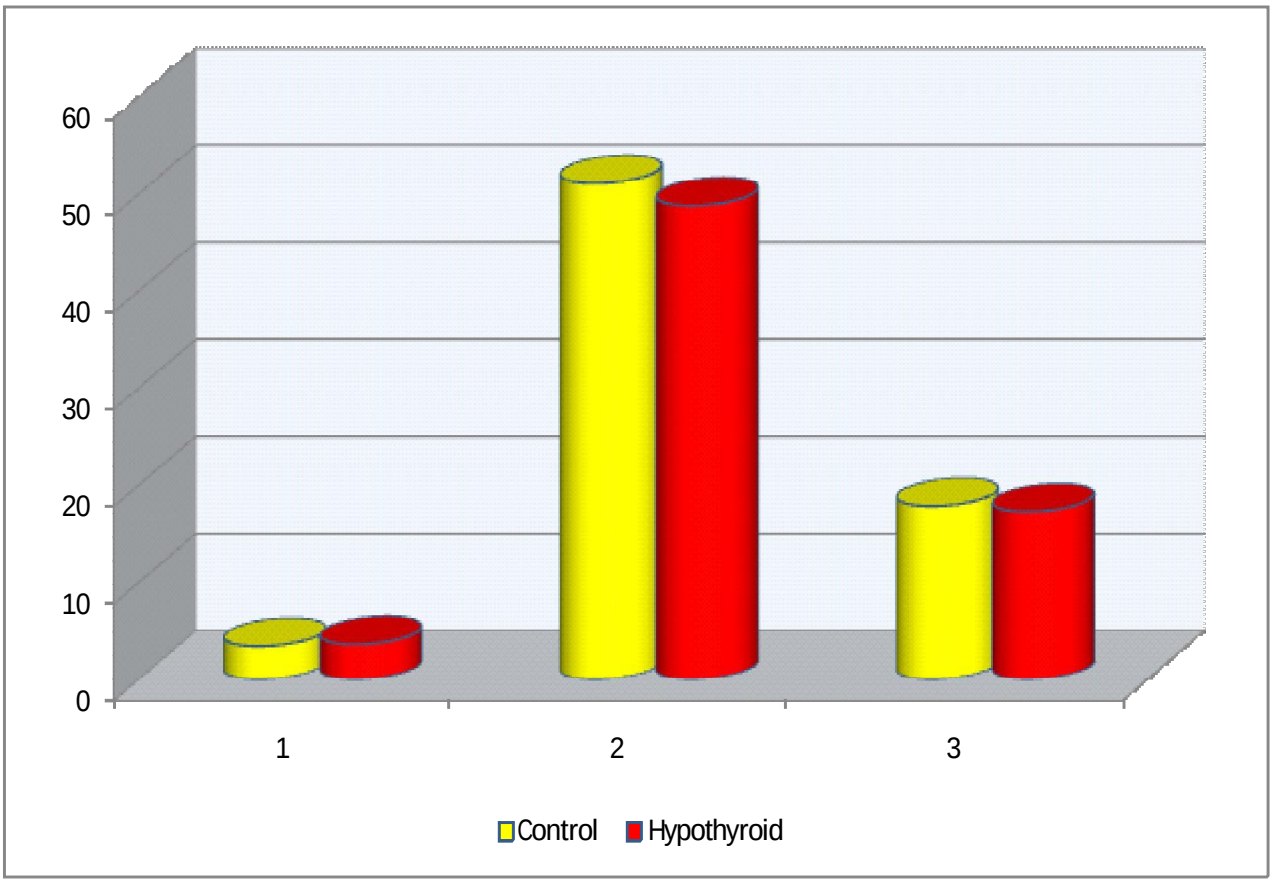
1-Latency 2-Conduction velocity 3-CMAP

TABLE 4: SENSORY CONUCTION OF ULNAR NERVE

Parameters	Control	Hypothyroid	'P' value
Latency(ms)	3.41 ± 0.19	3.6 ± 0.41	0.055
Conduction velocity (m/s)	51.09 ± 1.81	48.81 ± 3.07	0.004*
SNAP(µv)	17.84 ± 0.67	17.26 ± 2.06	0.220

***P value < 0.05 significant**

The above table on sensory conduction of the ulnar nerve indicated a non significant increase in the latency and decrease in the amplitude and a significant decrease in the conduction velocity in hypothyroid group.



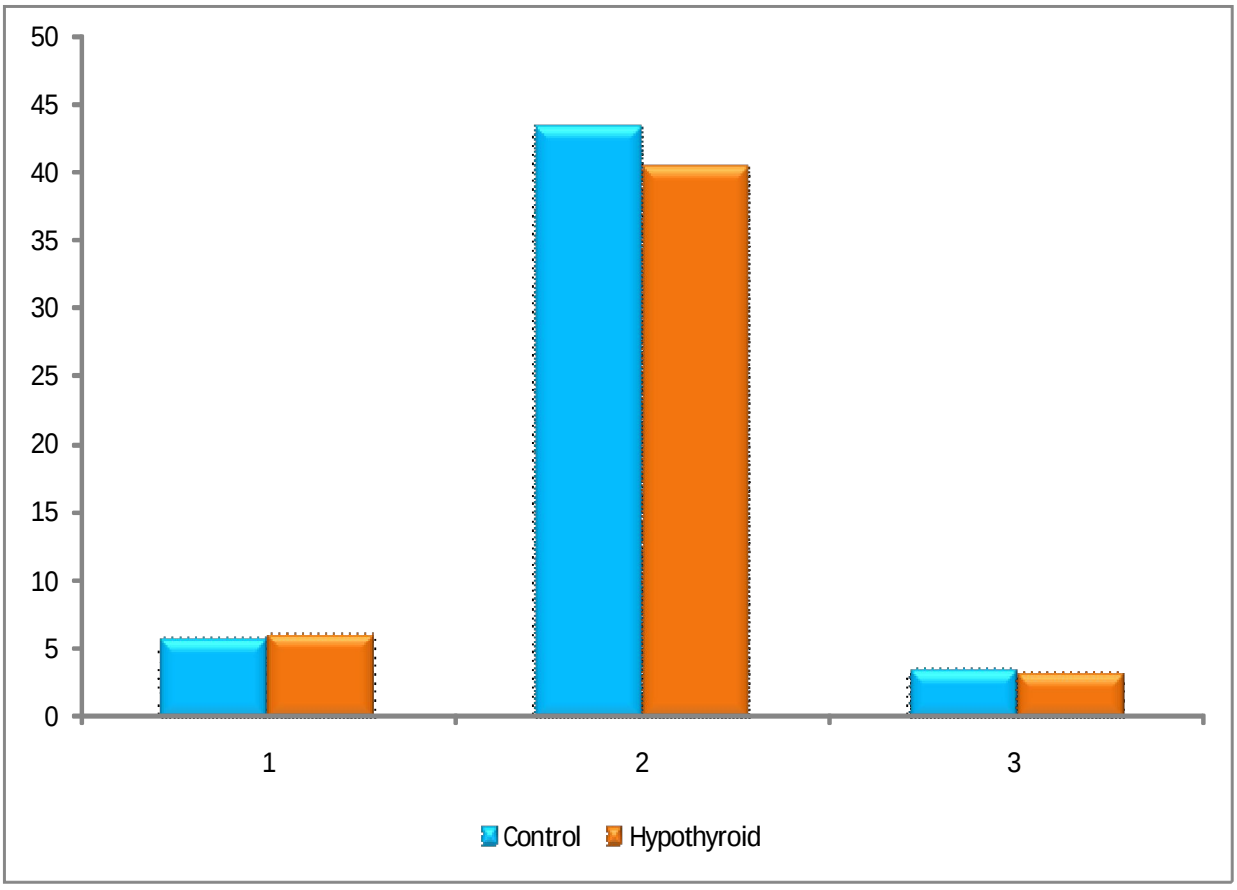
1-Latency 2-Conduction velocity 3.SNAP

TABLE 5: MOTOR CONUCTION OF TIBIAL NERVE

Parameters	Control	Hypothyroid	'P'value
Latency(ms)	5.82 ± 0.23	6.05 ± 0.56	0.93
Conduction velocity(m/s)	43.46± 2.02	40.55± 2.59	0.000*
CMAP(mV)	3.45 ±0.32	3.19 ± 0.75	0.13

***P value <0.05 significant**

The motor conduction parameters of the tibial nerve showed a significant decrease in the conduction velocity in hypothyroid group. The distal latency and compound motor action potential did not indicate a significant change.



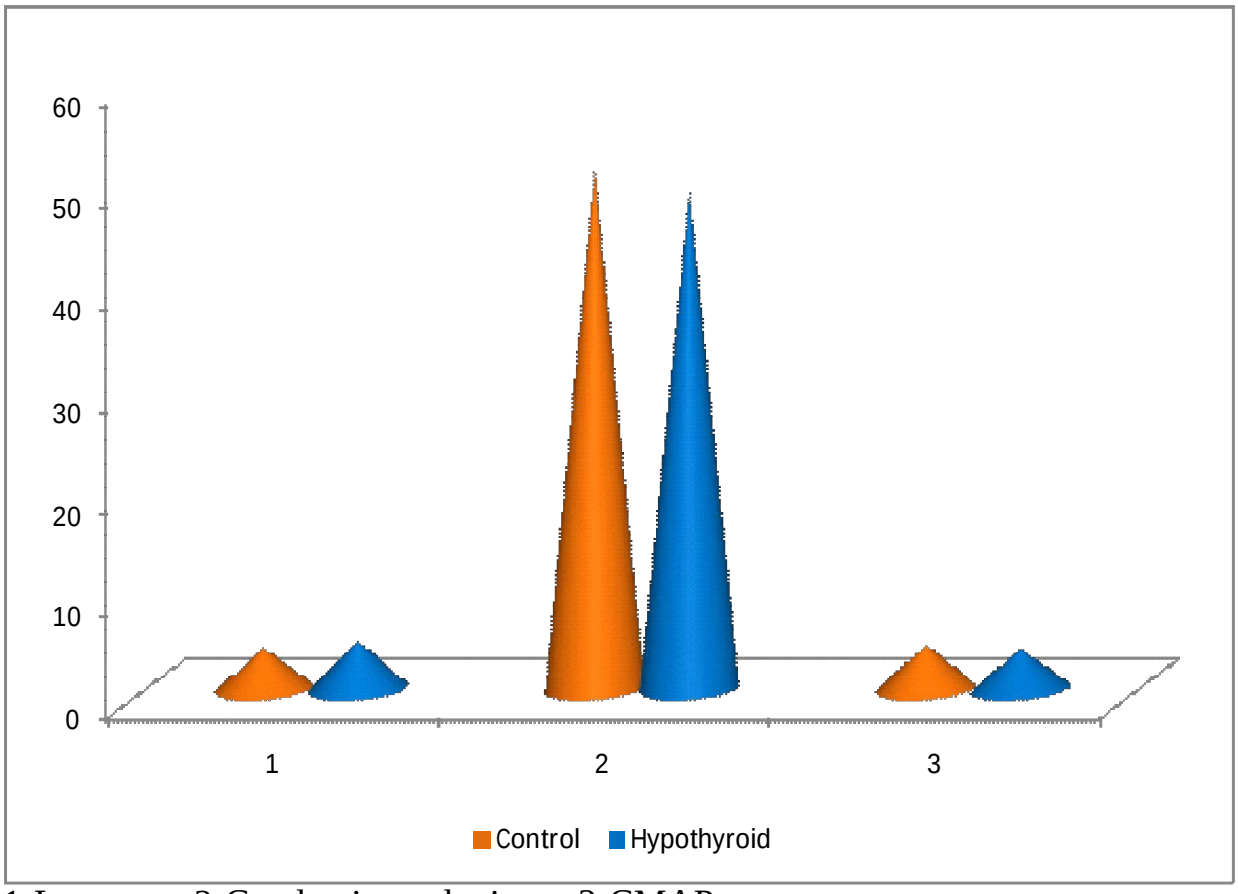
1-Latency 2-Conduction velocity 3-CMAP

TABLE 6: MOTOR CONUCTION OF MEDIAN NERVE

Parameters	Control	Hypothyroid	'P' value
Latency(ms)	4.03 ± 0.35	4.74 ± 0.82	0.001*
Conduction velocity (m/s)	51.01 ±1.87	48.83 ± 1.60	0.000*
CMAP(mV)	4.39 ± 0.26	3.99 ± 0.66	0.014*

*** P value <0.05 significant**

All the parameters in the median nerve motor conduction study were significantly altered in the hypothyroid group. The distal latency was increased and the conduction velocity and action potential was decreased.



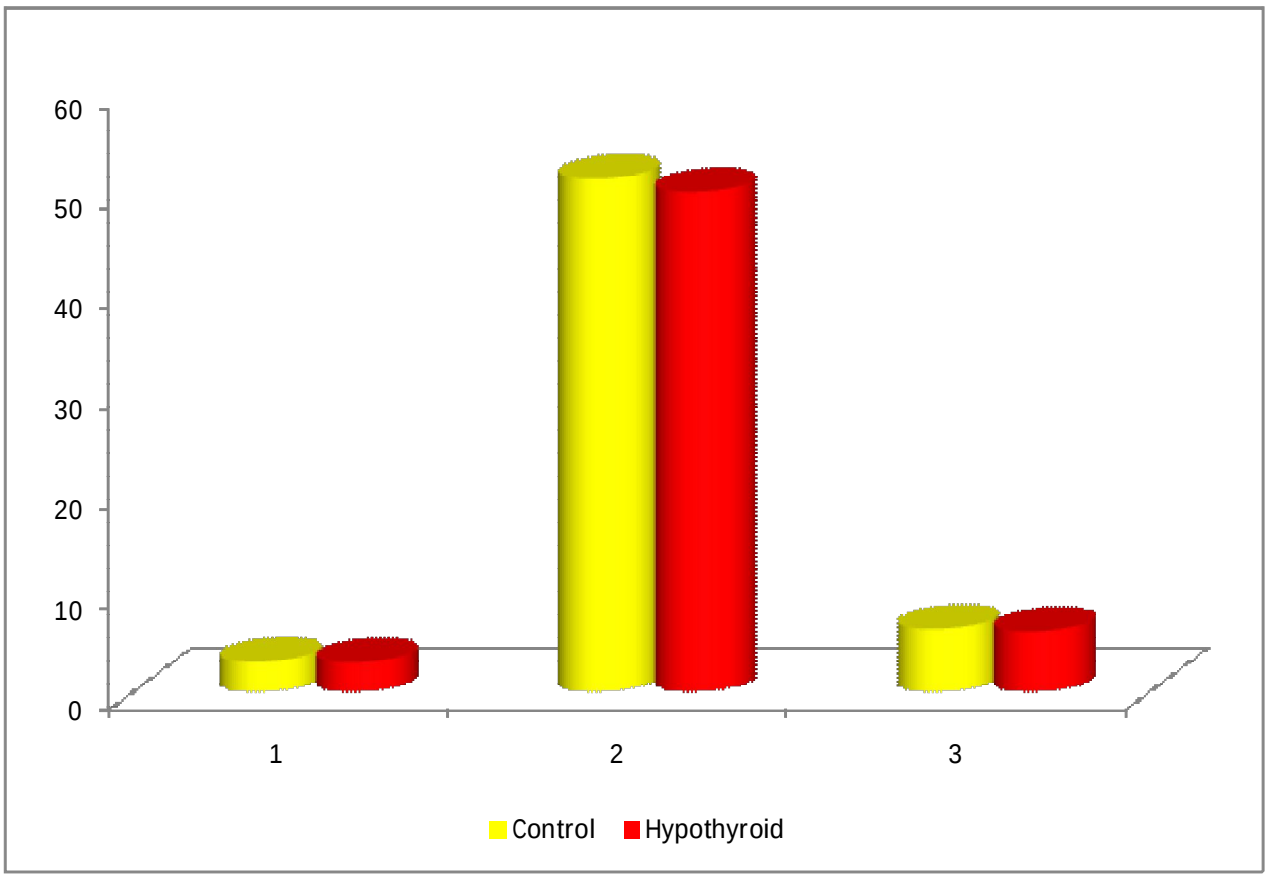
1-Latency 2-Conduction velocity 3-CMAP

TABLE 7: MOTOR CONUCTION OF ULNAR NERVE

Parameters	Control	Hypothyroid	'P' value
Latency(ms)	2.99 ± 0.26	2.93 ± 0.29	0.45
Conduction velocity(m/s)	51.14 ± 1.64	49.83 ± 2.85	0.67
CMAP(mV)	6.23 ± 0.23	5.99 ± 0.91	0.24

P value > 0.05 not significant

The ulnar nerve motor conduction study of the hypothyroid on comparision with control showed no statistically significant alteration of the nerve conduction parameters.



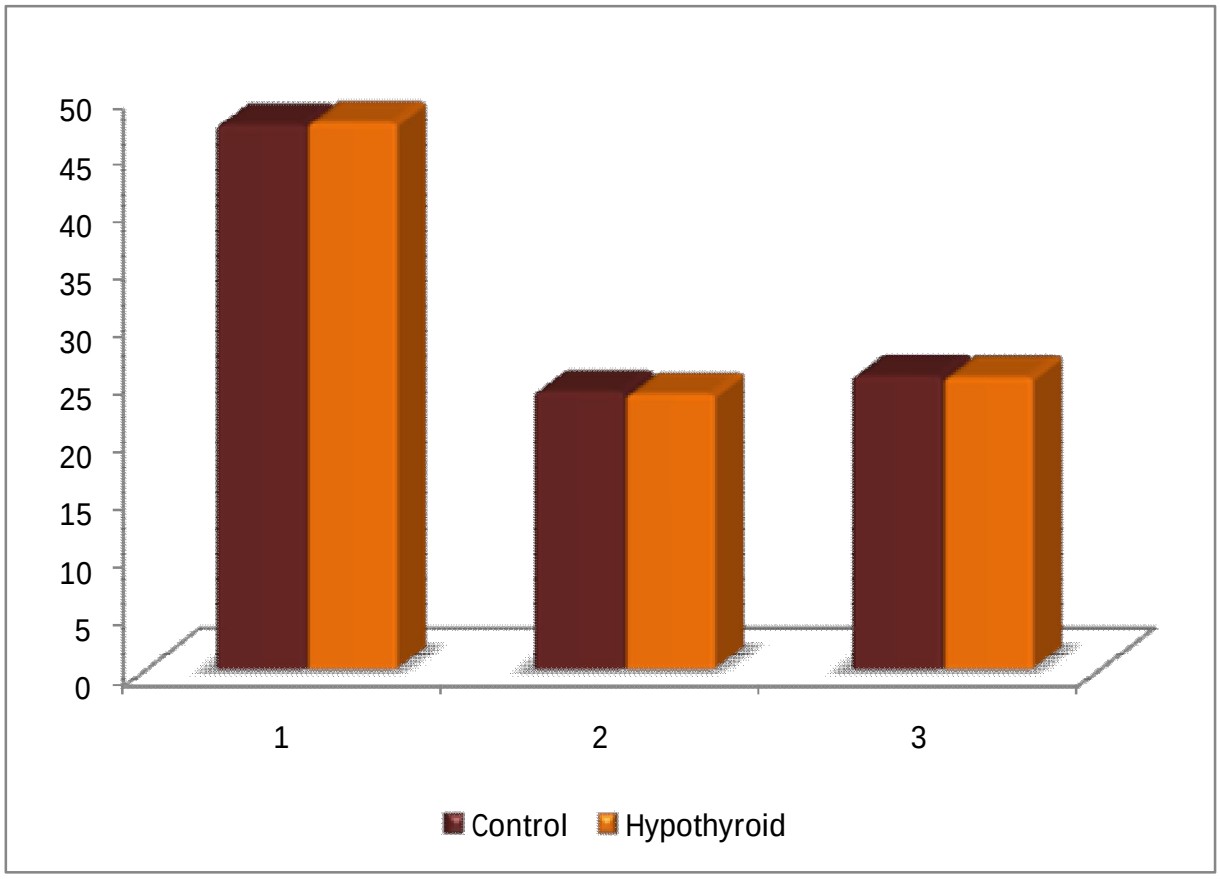
1-Latency 2-Conduction velocity 3-CMAP

TABLE 8: F WAVE LATENCY IN HYPOTHYROIDISM

Nerve	Control	Hypothyroid	P value
Tibial	47.26± 0.69	47.49±0.60	0.23
Median	24.1± 0.75	23.90±0.9	0.43
Ulnar	25.46±0.64	25.38±0.72	0.69

P value > 0.05 not significant

There was no significant change in F wave latency in hypothyroid group as compared to control.



1-Tibial nerve 2-Median nerve 3-Ulnar nerve

TABLE 9: NEUROPATHY IN HYPOTHYROIDISM

Neuropathy	No.. of hypothyroid	Percentage (%)
Sensory	10	45.4
Sensorimotor neuropathy	2	9
Carpal tunnel syndrome	8	36.3

The present study showed 45.4 % of patient had sensory neuropathy and 9 % and 36.3% of patients were affected by sensorimotor neuropathy and entrapment neuropathy in the form of carpal tunnel syndrome respectively.

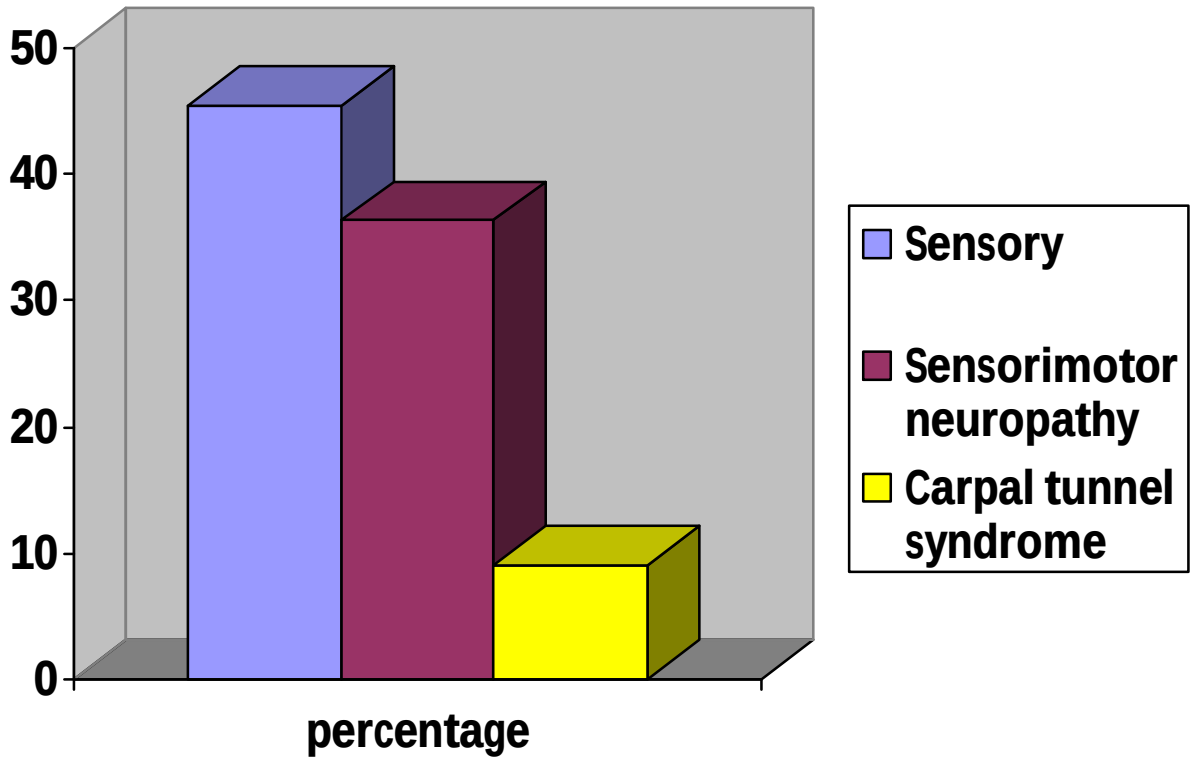
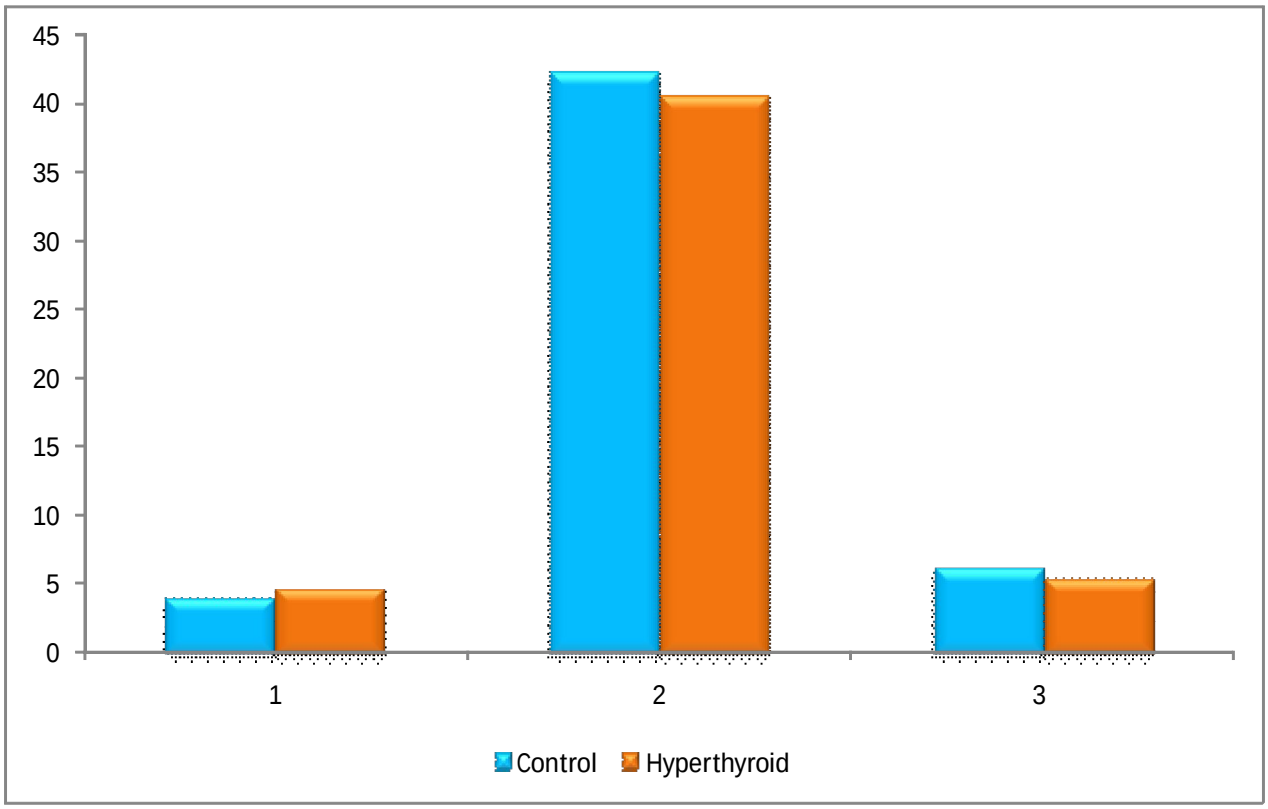


TABLE 10: SENSORY CONUCTION OF SURAL NERVE

Parameters	Control	Hyperthyroid	'P' value
Latency(ms)	3.97 ± 0.26	4.77 ± 0.67	0.000*
Conduction velocity(m/s)	42.2 ± 1.86	40.52± 2.42	0.02*
SNAP(µv)	6.2 ± 0.41	5.4 ± 0.74	0.000*

***P value <0.05 significant**

The sensory conduction studied in the hyperthyroid group showed a statistically significant increase in the latency and a decrease in the amplitude of the action potential. This study did not show a significant difference in the conduction velocity in both hyperthyroid and control group.



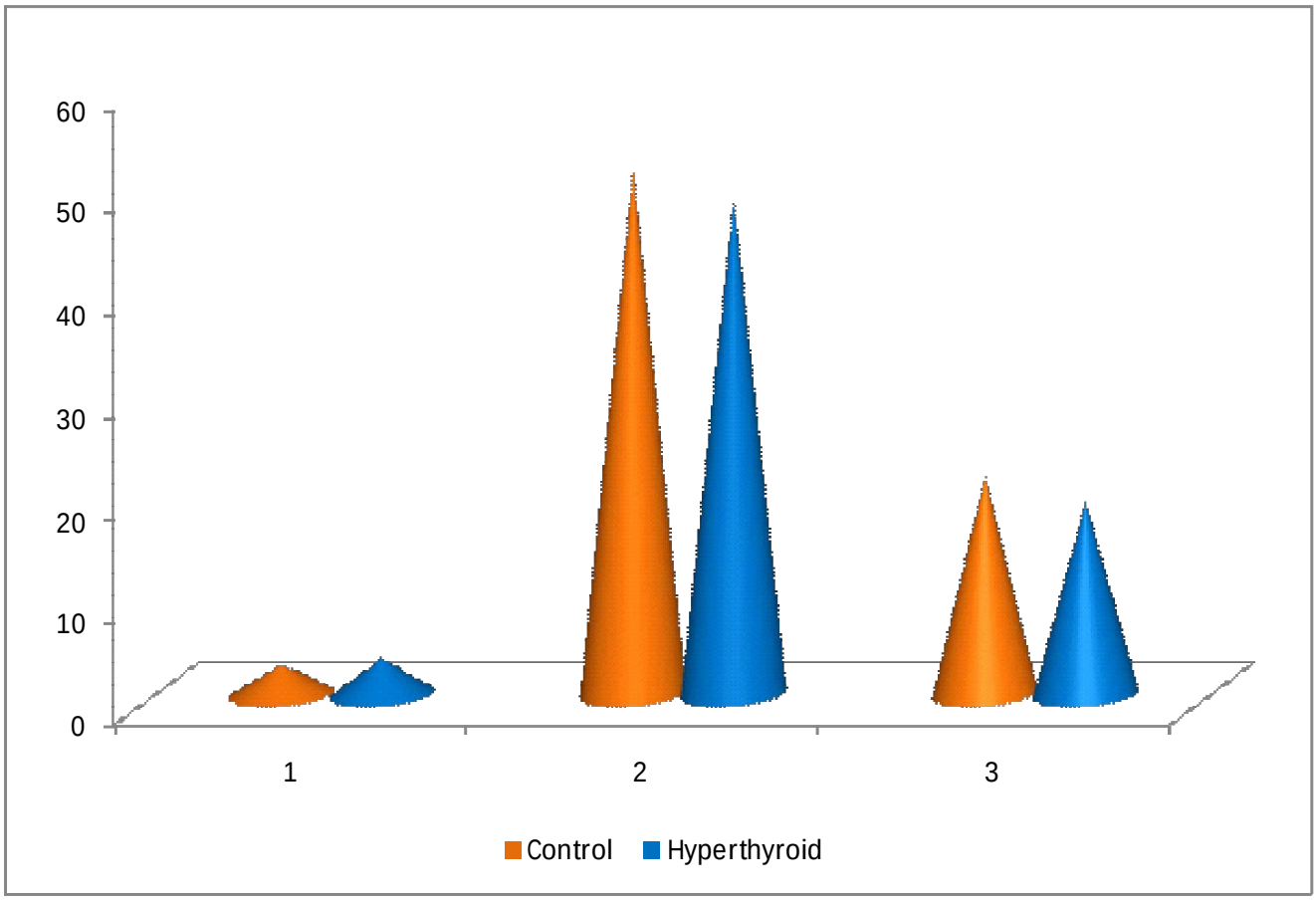
1-Latency 2-Conduction velocity 3.SNAP

TABLE 11: SENSORY CONUCTION OF MEDIAN NERVE

Parameters	Control	Hyperthyroid	'P' value
Latency(ms)	2.99 ± 0.19	3.58 ± 0.68	0.000*
Conduction velocity (m/s)	51.42 ± 1.56	48.55 ± 2.18	0.000*
SNAP(µv)	21.35 ± 1.39	18.88 ± 1.80	0.000*

***P value <0.05 significant**

In hyperthyroid individual all the sensory conduction parameters of median nerve showed significant changes. Latency was increased and conduction velocity and amplitude were decreased than that of control group.



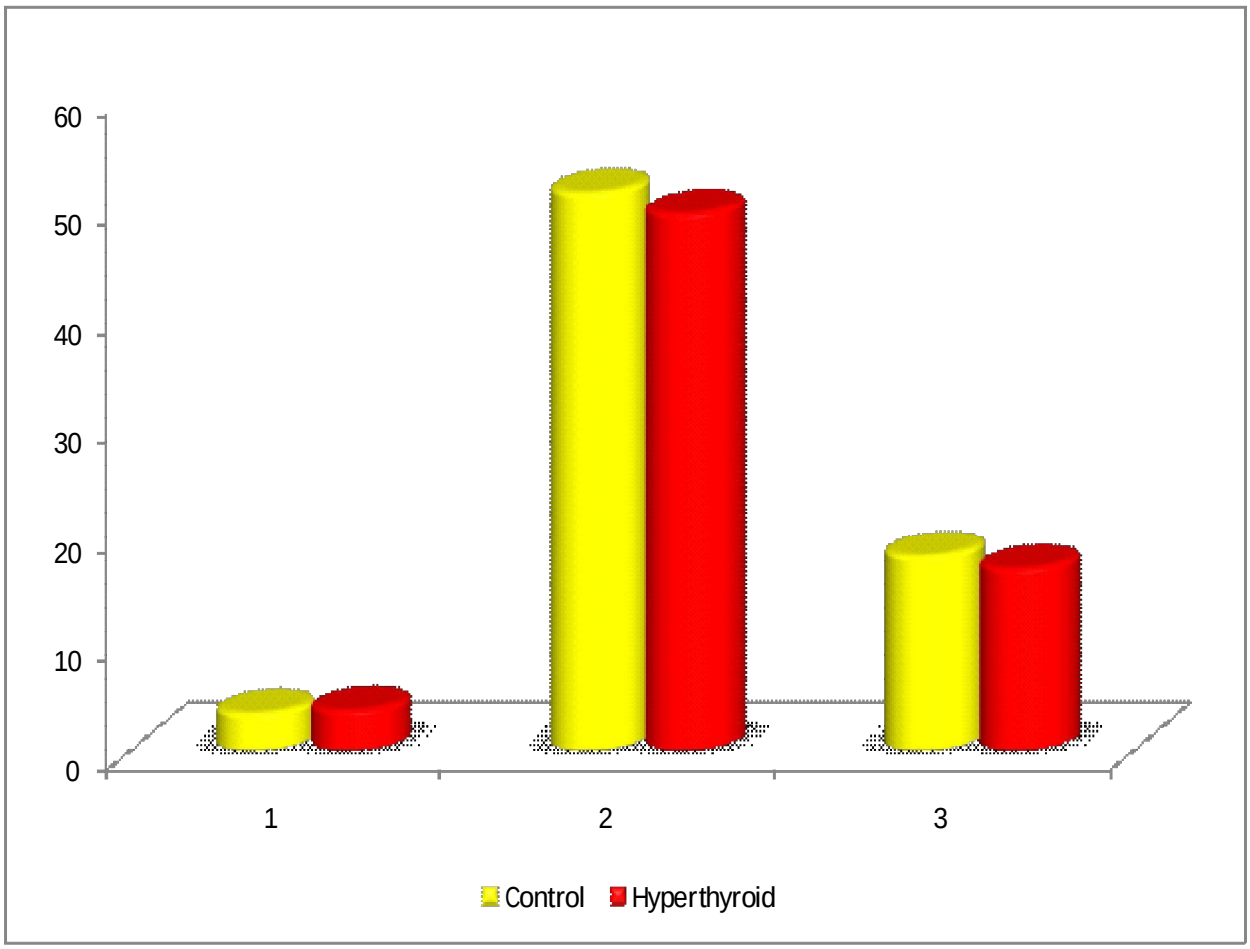
1-Latency 2-Conduction velocity 3.SNAP

TABLE 12: SENSORY CONUCTION OF ULNAR NERVE

Parameters	Control	Hyperthyroid	'P' value
Latency(ms)	3.41 ± 0.19	3.67 ±0.53	0.56
ConductionVelocity (m/s)	51.09± 1.81	49.18± 2.37	0.007*
SNAP(µv)	17.84± 0.67	16.7 ± 1.08	0.001*

***P value <0.05 significant**

The sensory conduction components of ulnar nerve showed significant decrease in the conduction velocity and amplitude. But no difference was observed in the latency in the hyperthyroid group as compared with controls.



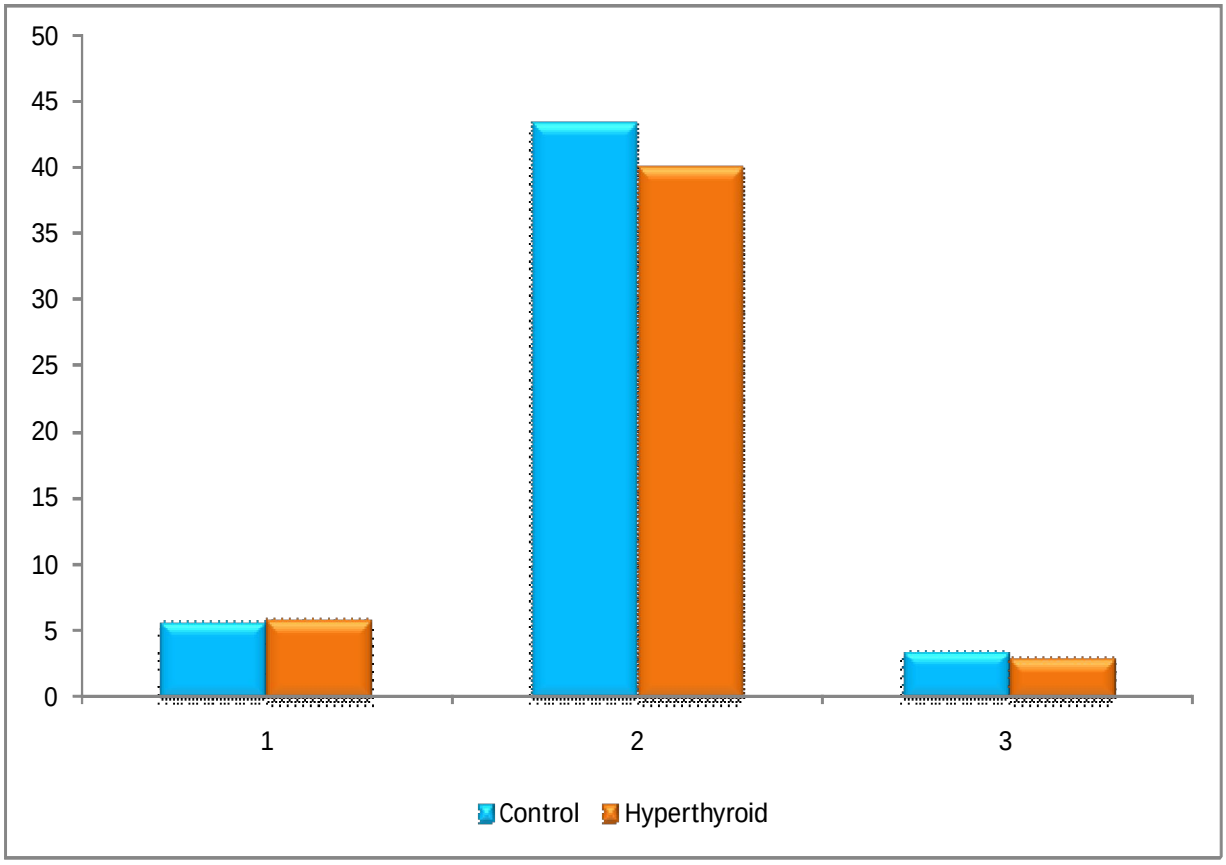
1-Latency 2-Conduction velocity 3.SNAP

TABLE 13: MOTOR CONUCTION OF POSTERIOR TIBIAL NERVE

Parameters	Control	Hyperthyroid	'P'value
Latency (ms)	5.82±0.23	5.877±0.46	0.66
Conductionvelocity(ms)	43.46±2.2	40.06 ± 1.64	0.000*
CMAP(mV)	3.45±0.32	3.078± 0.66	0.038*

***P value <0.05 significant**

The conduction study of the posterior tibial nerve in hypothyroid group showed significant reduction in amplitude and conduction velocity. The alteration in distal latency parameter was not significant.



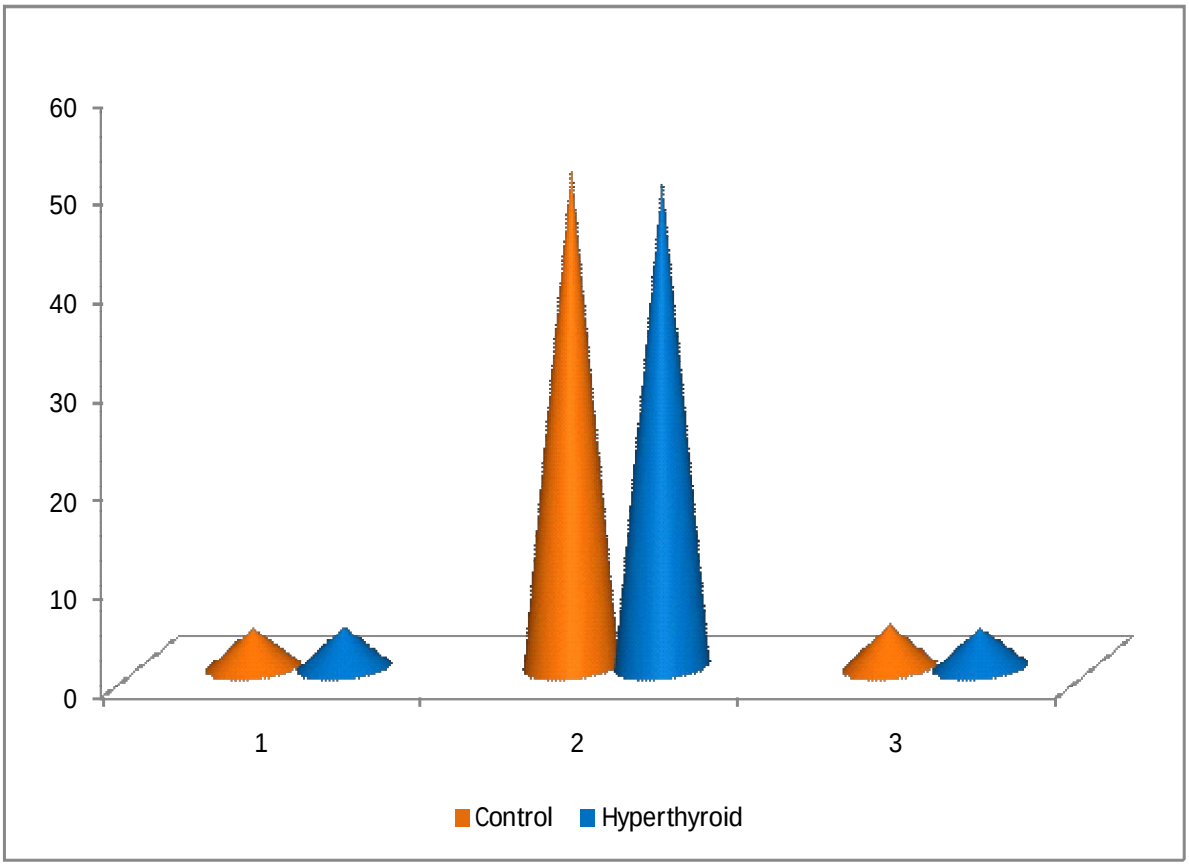
1-Latency 2-Conduction velocity 3-CMAP

TABLE 14: MOTOR CONUCTION OF MEDIAN NERVE

Parameters	Control	Hyperthyroid	'P' value
Latency(ms)	4.03 ± 0.35	4.16± 0.77	0.49
Conduction velocity(m/s)	51.01 ± 1.87	49.70±3.37	0.14
CMAP(mV)	4.39 ± 0.26	4.05 ± 0.82	0.107

P value >0.05 not significant

The distal latency, conduction velocity and CMAP of motor conduction study of median nerve did not exhibit a significant change in hyperthyroid group as compared to control group



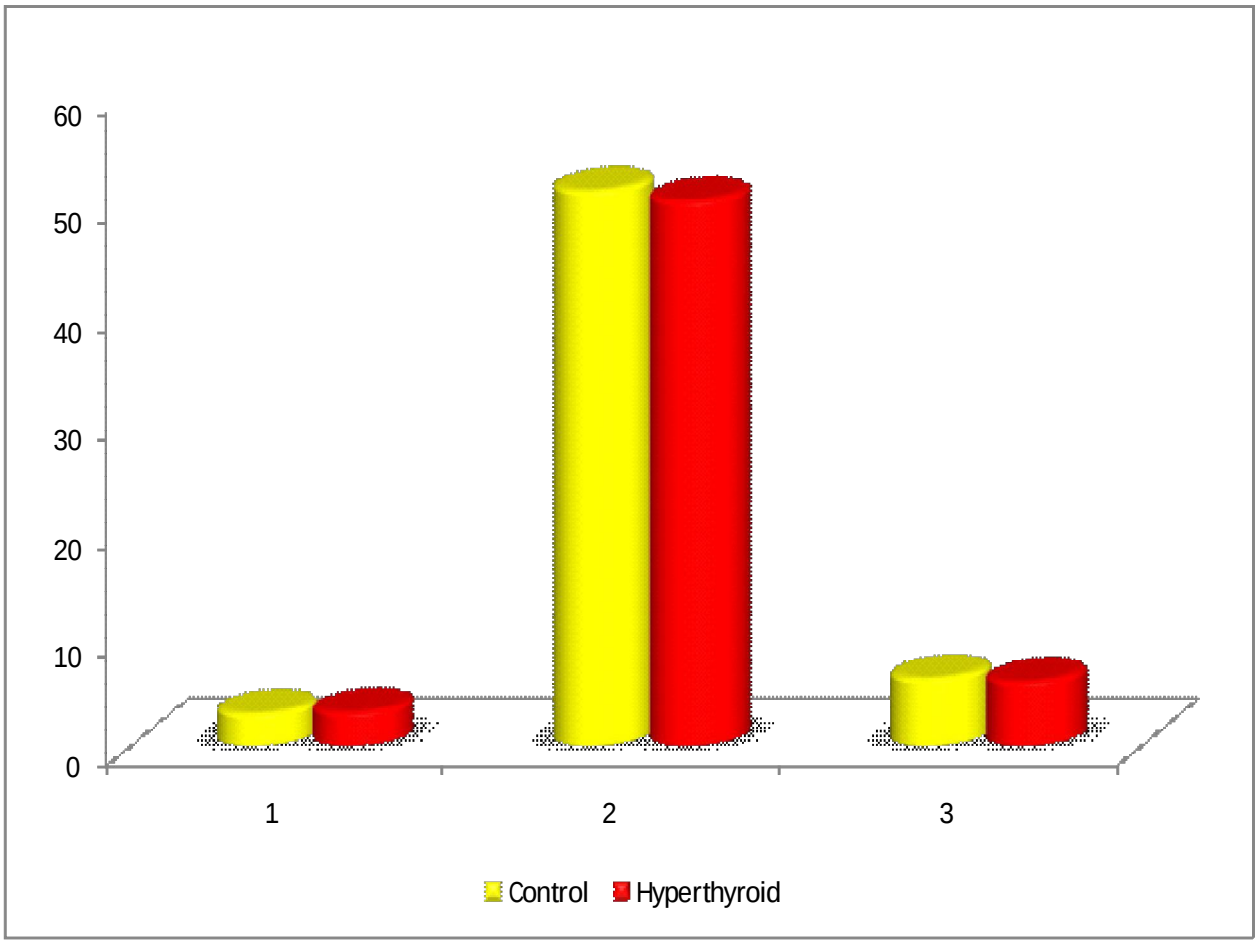
1-Latency 2-Conduction velocity 3-CMAP

TABLE 15: MOTOR CONUCTION OF ULNAR NERVE

Parameters	Control	Hyperthyroid	'P' value
Latency(ms)	2.99 ± 0.26	3.11 ± 0.29	0.181
Conduction velocity(m/s)	51.14 ± 1.64	50.21± 1.65	0.078
CMAP(mV)	6.23 ± 0.23	5.95±1.24	0.362

P value >0.05 not significant

The values of motor conduction study of ulnar nerve showed no significant alteration of distal latency, conduction velocity and CMAP in hyperthyroid group as compared to control group.



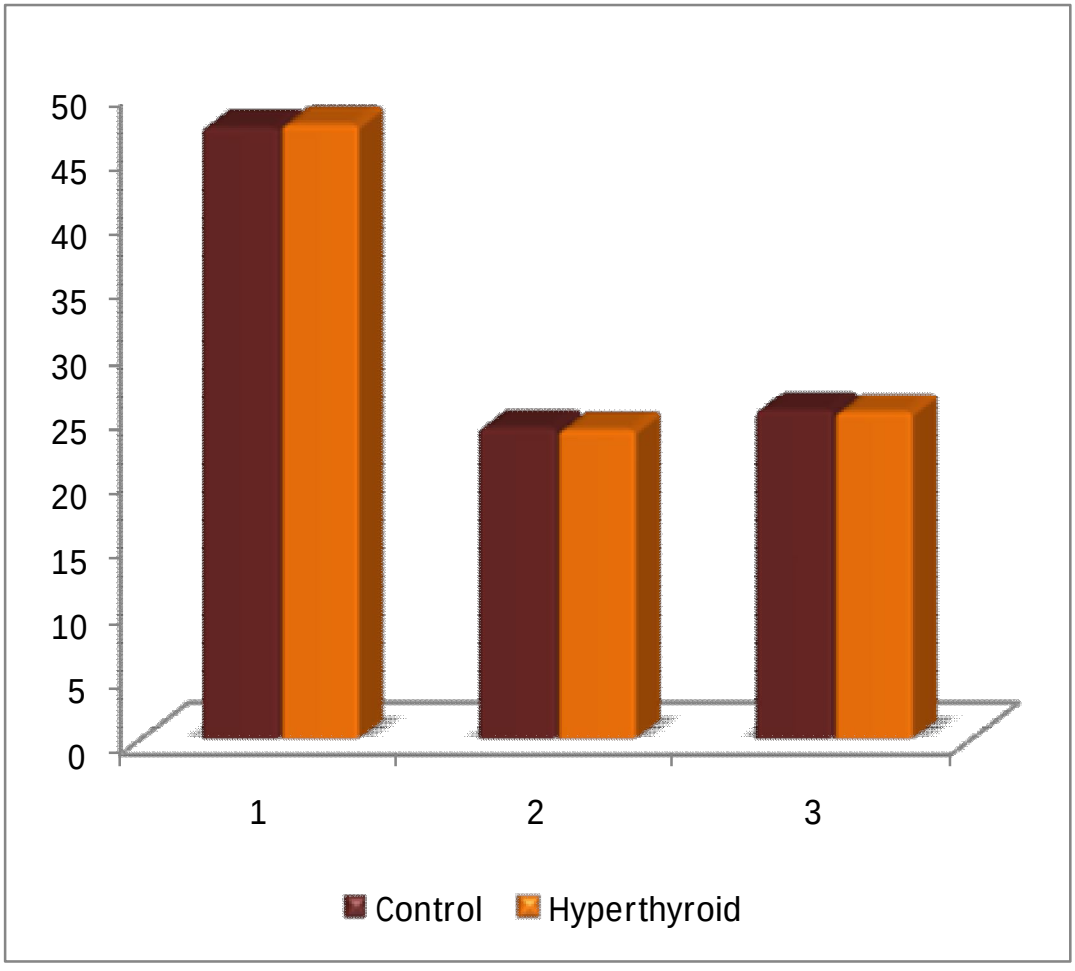
1-Latency 2-Conduction velocity 3-CMAP

TABLE 16:F WAVE LATENCY IN HYPERTHYROIDISM

Nerve	Control	Hyperthyroid	P value
Tibial	47.26± 0.69	47.50±0.61	0.24
Median	24.1± 0.75	23.96±0.86	0.60
Ulnar	25.46±0.64	25.34±0.61	0.55

P value >0.05 not significant

There was no significant change in F wave latency in hyperthyroid group as compared to control.



1-Tibial nerve 2-Median nerve 3-Ulnar nerve

TABLE 17: NEUROPATHY IN HYPERTHYROIDISM

Neuropathy	No. of hyperthyroid	Percentage (%)
Sensory	11	61.1
Sensorimotor Neuropathy	1	5.5
Carpal tunnel syndrome	3	16.6

61.1 % of patient had sensory neuropathy and 5.5 % and 16.6% of patients were affected by sensorimotor neuropathy and entrapment neuropathy in the form of carpal tunnel syndrome respectively.

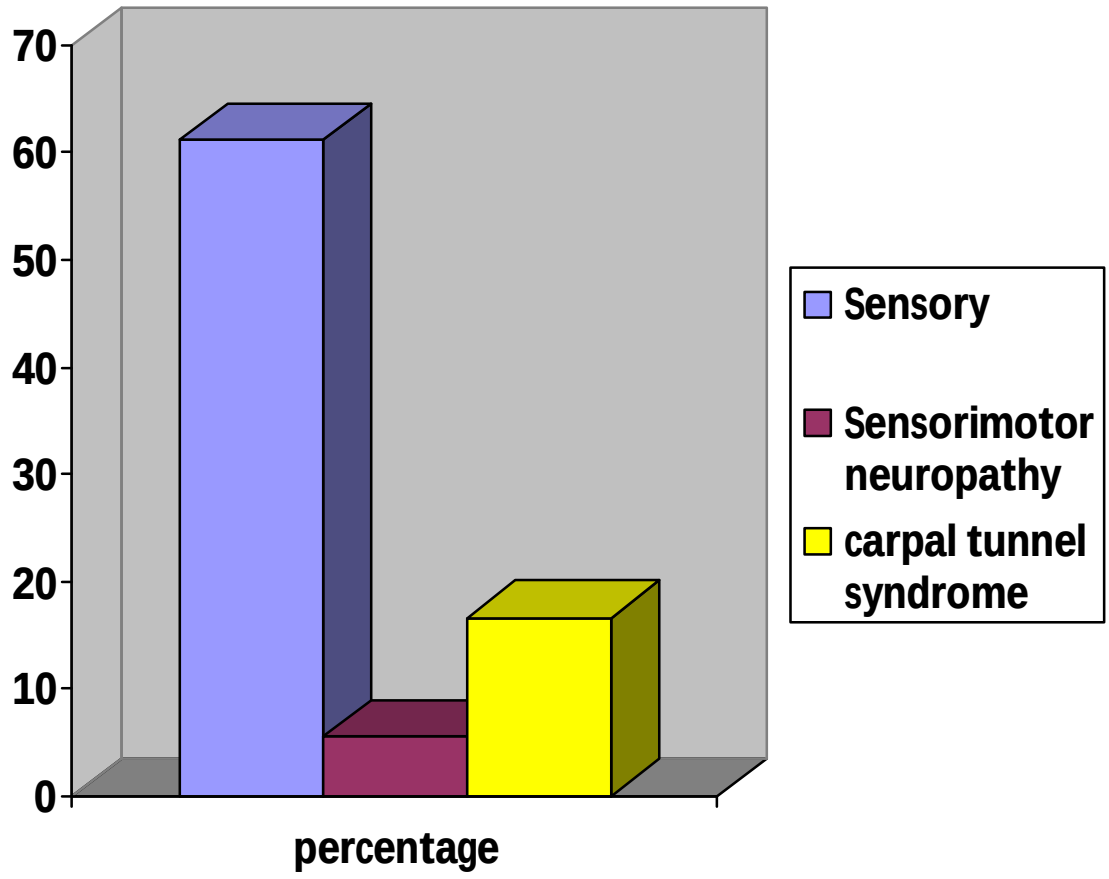
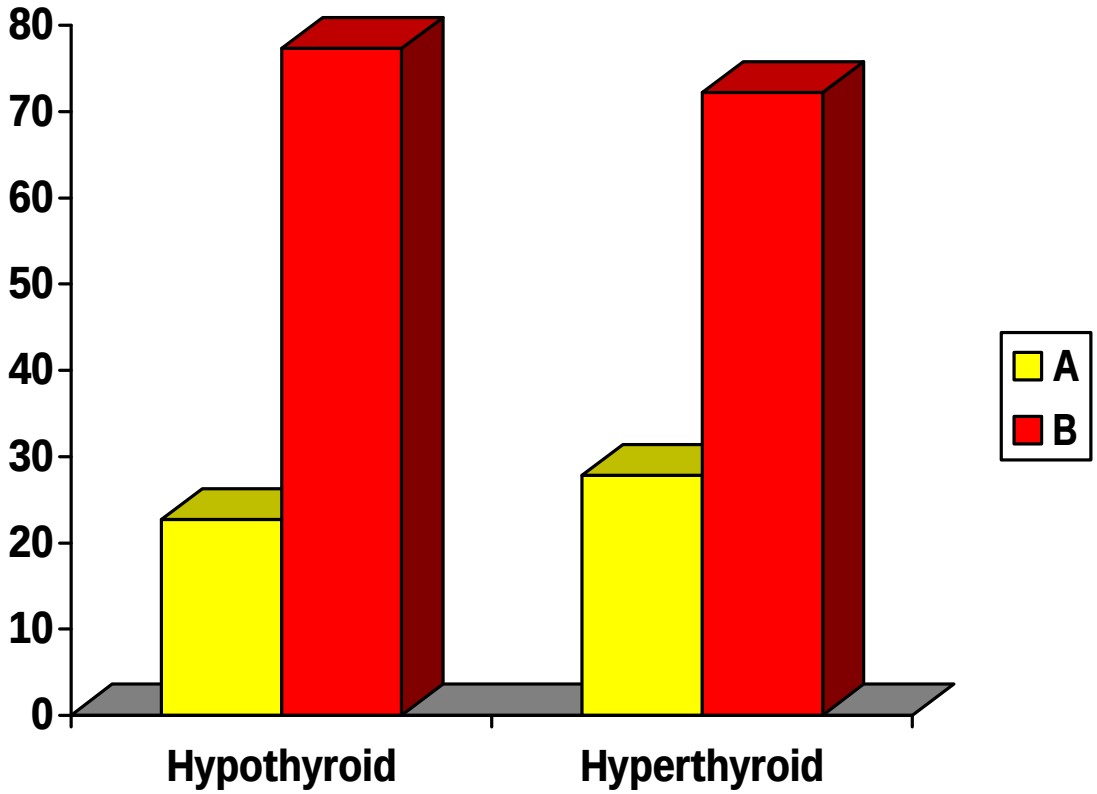


TABLE 18: DURATION OF SYMPTOMS OF THYROID DISORDERS

Group	Hypothyroid	Hyperthyroid
A	5 (22.7%)	5 (27.8 %)
B	17 (77.3%)	13 (72.2%)

Patients in hyperthyroid and hypothyroid group were subgrouped into two based on the duration of symptoms.Group A & B consisted of patients with symptoms upto 6 months and more than 6 months respectively. In this study most of the patients were in group B.



DISCUSSION

In the present study, the nerve conduction was performed in 22 hypothyroid, 18 hyperthyroid and 25 normal individuals. The person was diagnosed to have peripheral neuropathy if two or more nerves are involved. Prolonged latency in sensory conduction study indicates sensory neuropathy. In motor conduction study, decrease in amplitude denotes axonal degeneration and prolonged distal latency and conduction velocity indicate demyelination. Carpal tunnel syndrome is indicated by the significant prolongation of distal latency.

STUDY OF HYPOTHYROIDISM:

Hypothyroidism is most commonly due to autoimmune pathology and it has got a slow progressive course. In the present study, sensory conduction parameters of median and sural nerve showed statistically significant values. These findings are supported by studies by many researchers including Khedr et al[87] and Ihsan M.Ajeena et al[75]. Adikesavan et al[86] agrees the finding with the sural nerve and conduction velocity of median nerve but disagreeing the latency and amplitude changes. The ulnar nerve conduction study did not detect any significant change in the parameters except conduction velocity .This finding is consistent with the Ihsan M.Ajeena et al and Yeasmin et al [76]. Gulbun Yuskel et al[80] has found a significant change in ulnar nerve action potential, a finding not consistent with the present and most of the studies.

Motor conduction parameters showed the significant change in the median nerve. The finding of my study is similar with study by Sabina Yeasmin

et al [81] and Ihsan M.Ajeena et al. Insignificant change in the parameter is the observation by Hala S Sweed et al[73] in median nerve. The tibial nerve (except conduction velocity) and ulnar nerve parameters did not indicate a significant change. This finding correlates with many of the studies performed. No significant change in F wave latency in any of the nerve was noted in our study. Many of the above mentioned studies agree with this finding. Involvement of motor component of the median nerve might be due to the long duration of symptoms in most of the patients in hypothyroid group.

Combining all parameters, the present study had shown the presence of sensory neuropathy in 45.4 % of and sensorimotor neuropathy in 9.1% of the hypothyroid group studied. These finding are in consistent with the observation reported by the Ihsan M.Ajeena et al and Gulbun Yuskel et al. Carpal tunnel syndrome is present in 36 % of the hypothyroid group. The incidence of carpal tunnel syndrome in hypothyroidism by various investigators ranges from 5 to 92 %. Marcia W Cruz et al have reported 43.7% as the incidence of CTS. The result of my study is comparable with this finding. [88]

Thyroid hormone plays a key role in the regulation of basal metabolism. By its influence on metabolism, it enhances the nerve conduction by its various effects on nervous system. In hypothyroidism, due to decreased level of the hormone, there is a reduction in the functional capacity of Na^+- K^+ pump because of suppressed ATP production. Axonal transport requires the optimum functioning of this pump. This reduction in axonal transport causes a significant

change in the nerve conduction. For unknown reason, hypothyroidism affects the sensory nerves earlier than the motor nerves. The distal nerves like median and sural nerves show changes earlier than the proximal nerves. Demyelination and axonal degeneration happens due to the oxidative injury of myelinated fibers. Axonal degeneration is the common cause of neuropathy in the present study. In addition, low temperature and low sodium level in hypothyroidism also affect the conduction parameters. In hypothyroidism, there occurs reduction in the degradation of the mucopolysaccharide and carpal tunnel syndrome is a consequence of the deposition of mucopolysaccharide.

STUDY OF HYPERTHYROIDISM:

Hyperthyroidism common in females is also most commonly due to autoimmune disorders and is slowly progressive over a period of time. The present author had observed a significant prolongation of latency of the sensory conduction of the median and sural nerve. This finding resembles the observations made by Hala et al and Ihsan M.Ajeena et al. Gulbun Yuskel et al agrees the sural nerve latency changes but not in favour of changes in the median nerve latency. Latency of sensory conduction of ulnar nerve showed no significant results. This finding is significantly similar in most of the study.

Motor conduction study of the nerves except tibial nerve in the present study showed no significant change. This is in consistent with Ihsan M.Ajeena et al except for tibial nerve. Gulbun Yuskel et al have found out a significant reduction in conduction velocity in tibial nerve study. This finding is not

consistent with the study conducted by Hala et al. who have observed the significant changes in the above nerves except conduction velocity of the ulnar nerve and distal latency of the median nerve. The predominant involvement of sensory than motor nerve in hyperthyroidism has been reported in the literature by Ruurd F Duyff [84]. No significant change in F wave latency in any of the nerve was noted in our study. Many authors agree with this finding. Longer duration of the symptoms in most of the patients of the hyperthyroid group is a probable reason for involvement of tibial nerve.

To summarise, the present study had found the presence of sensory neuropathy in 61 %, sensory motor neuropathy in 5.5% and carpal tunnel syndrome in 17 % of hyperthyroid individuals. Ihsan M.Ajeena et al agree with the incidence of sensorimotor neuropathy. The incidence of carpel tunnel syndrome and sensorineuropathy is comparable with the study by Hala et al. The state of increased basal metabolic rate in hyperthyroidism is the proposed hypothesis for axonal type of polyneuropathy.

SUMMARY AND CONCLUSION

Thyroid disorders having an indolent course affect all the body systems. The manifestations of each system occur after a particular level of pathophysiological changes.

- ✓ In the centre of the present study, no previous research has been adopted to find out the neurological changes by means of electrodiagnostic studies. The primary aim of the nerve conduction studies is to identify the presence of neuropathy before the obvious clinical manifestations call for the attention of the treating physician.
- ✓ The present study conducted with 22 hypothyroid, 18 hyperthyroid and 25 normal individuals showed that the neuropathy was common finding in thyroid disorders.
- ✓ Sensory neuropathy was present in about 45.4 % of hypothyroid and 61 % of hyperthyroid individuals. Earlier occurrence of the neuropathy in sensory and distal nerves is evident from the median and sural nerve sensory conduction parameters.
- ✓ Sensorimotor neuropathy was present in 9.1 % of the hypothyroid and 5.5 % of the hyperthyroid group.
- ✓ Carpal tunnel syndrome was observed in 36 % of hypothyroid and 17 % of the hyperthyroid patients. The presence of carpal tunnel syndrome in significant number of individual in both groups proves the use of nerve conduction study in the asymptomatic individuals.

CONCLUSION:

This study has enlightened the importance of the nerve conduction study in patients with thyroid disorders. Earlier study has shown the presence of hypothyroidism in previously operated cases of carpal tunnel syndrome. We have also learnt that institution of treatment in hyperthyroidism has reversed the features of carpal tunnel syndrome and persistence of the clinical features in inadequately treated hypothyroid. This alerts the physicians to perform thyroid assay before deciding the mode of treatment and also to undertake nerve conduction study in individuals with long standing thyroid disorders especially hypothyroidism.

FUTURE STUDY PLAN

This study is of public health importance in identifying the earlier diagnosis of neuropathy in thyroid disorder especially hypothyroid. The planned future studies by the author are

- To study the effect in both sexes
- To correlate the results of conduction parameters before and after the treatment.
- To compare the duration of disease with the changes
- To perform comparative study of the thickness of the carpal tunnel using radiological methods and the nerve conduction studies
- To study the central nervous system involvements by using various evoked potential study.
- Cognitive impairment in hypothyroid children.

BIBLIOGRAPHY

1. Parveen Kumar & Michael Clark - Kumar & Clark's Clinical Medicine 7th ed. P,982-994
2. Kececi H , Degirmenci Y et al - Hormone replacement therapy in hypothyroidism and nerve conduction study. Neurophysiol Clin. 2006 Mar-Apr; 36(2):79-83. Epub 2006 Apr 25
3. Timeline - American Thyroid Association - updated October 5, 2013 p1-8
4. History of the thyroid gland –http://www.endocrinesurgeon.co .uk/index.php/the-history-of-the-thyroid-gland
5. Charles Robert Harigton et al-Chemistry of thyroxine- Biochem J 1927: 21(1:) - 169-183
6. Ronald C. Hamdy The Thyroid Gland: A Brief Historical Perspective South Med J. 2002;95(5)
7. T. W. Sadler - Langman's Medical Embryology 9th ed .p 384-386
8. Sarada Subramaniam – Textbook of human physiology -6 th ed –page 486-496 & 651-663
9. Bruce M. Koeppen, Bruce A Stanton Bern & Levy Physiology -6th ed – pages 53-82 &726-737
10. Christine Spitzweg et al, Sodium Iodide Symporter (NIS) and Thyroid-HORMONES 2002, 1(1):22-34.

11. Jean Ruf et al -Structural and functional aspects of thyroid peroxidise- Archives of Biochemistry and Biophysics Volume 445, Issue 2, 15 January 2006, Pages 269–277
12. Francoise Miot et alThyroid Hormone Synthesis and Secretion- Thyroid Disease Manager- Last Updated: December 26, 2012
13. Marino M et al - Role of megalin (gp330) in transcytosis of thyroglobulin by thyroid cells. A novel function in the control of thyroid hormone release. J Biol Chem. 2000 Mar 10;275(10):7125-37.
14. Wendy M van der Deure et al - Molecular aspects of thyroid hormone transporters, including MCT8, MCT10, and OATPs, and the effects of genetic variation inthese transporters - J Mol Endocrinol January 1, 2010 44 1-11
15. Kohrle J. -Thyroid hormone deiodinases--a selenoenzyme family acting as gatekeepers to thyroid hormone action.- Acta Med Austriaca. 1996;23(1-2):17-30.
16. Kim E. Barrett, Susan M. Barman, Scott Boitano,Heddwen L. Brooks,- Ganong's Review Of Medical Physiology -24 th ed- pages 83-96& 339-352
17. Guyton & Hall-Text book of Medical Physiolgy-12th ed-pages 57-70& 559-564& 907-918
18. Fernando Goglia Thyroid Hormones and Mitochondria- Bioscience Reports, Vol. 22, No. 1, February 2002 (© 2002)

19. A J Forhead et al - Thyroid hormones in fetal growth and prepartum maturation- J Endocrinol June 1, 2014 221 R87-R103
20. Chidakel A et al - Peripheral metabolism of thyroid hormone and glucose homeostasis.- Thyroid. 2005 Aug; 15(8):899-903.
21. Irwin Klein,- Thyroid Disease and the Heart- Circulation. 2007; 116: 1725-1735
22. Schlenker EH - Effects of hypothyroidism on the respiratory system and control ofbreathing: Human studies and animal models- Respir Physiol Neurobiol. 2012 Apr 30;181(2):123
23. W R Middleton- Thyroid hormones and the gut - Gut. Feb 1971; 12(2): 172–177.
24. Rajender Singh et al - Thyroid Hormones in Male Reproduction and Fertility- The Open Reproductive Science Journal, 2011, 3, 98-104
25. S Chan- Thyroid hormone and central nervous system development- Journal of Endocrinology (2000) 165, 1–8
26. Walter F .Boron & Emile L. Boulpaep -Medical Physiology- Updated 2 nd ed.pages 179-211&267-274&310-322&1044 to1056
27. Johannes W. Dietrich et al –TSH and Thyrotrophic agonists: Key actor in thyroid homeostasis- Journal of Thyroid Research volume 2012 article ID 351864 ,29 pages.
28. G. K. Pal :Text book of medical Physiology 2 nd ed.pages 153-69& 352-366

29. Perl E.- The 1944 Nobel Prize to Erlanger and Gasser - FASEB J. 1994 Jul;8(10):782-3.

30. Christof J. Schwiening- A brief historical perspective: Hodgkin and Huxley - June 1, 2012 The Journal of Physiology, 590, 2571-2575

31. WilliamCobb and John Marshall- Repetitive discharges from human motor nerves after ischaemia and their absence after cooling- j. neurol. neurosurg. psychiat, 1954, 17, 183.

32. G. D. Dawson - The relative excitability and conduction velocity of sensory and motor nerve fibres in man J Physiol. Feb 28, 1956; 131(2): 436–451.

33. Indu Khurana- Text book of Medical Physiology-1st ed 915 to 942 and 1010-1061

34. R.L.Bijlani- Understanding Medical Physiology – 4th ed 507 -513 & 561-564.

35. A K Jain –Textbook of Physiology-5 th ed pages 877-904 and 917-936.

36. Cyril A Keele et al-Sampson & Wright's applied physiology -13th ed- pages 260-277 &287-90&537-46

37. O.P.Tandon & Y. Tripathi et al - Best & Taylor's Physiological Basis of Medical Practice -13th ed – pages 37 – 62 & 855-65

38. J. M. Ritchie -On the Relation between Fibre Diameter and Conduction Velocity inMyelinated Nerve Fibres -Proceedings of the Royal Society of London. Series B, Biological Sciences Vol. 217, No. 1206 (Dec. 22, 1982), pp. 29-3

39. Taylor Chomiak - What Is the Optimal Value of the g-Ratio for Myelinated Fibers in the Rat CNS?A Theoretical Approach-November 13, 2009 DOI: 10.1371/journal.pone.0007754

40. U K Misra and Khalida -Clinical Neurophysiology-2nd ed- pages 1to 112

41. Michael J Aminoff - Electrodiagnosis in clinical neurology - 5 th ed page 285 -366

42. Colin D.Binnie et al – Clinical Neurophysiology -1 st ed – pages 1-75

43. A Mallik, Nerve conduction studies: essentials and pitfalls in practice- *J Neurol Neurosurg Psychiatry* 2005;76:suppl 2 ii 23-ii3

44. Jun Kimura - Principles and Pitfalls of Nerve Conduction Studies-Annals of Neurology Vol 16 No 4 October 1984

45. Dhavalikar- Effect of Skin Temperature on Nerve Conduction Velocity and Reliability of Temperature Correction Formula in Indian Females- Journal of Exercise Science and Physiotheraphy.-vol 5.no..1 ;24-29, 2009*J*

46. James B Caress-Technical, Physiological and Anatomic Considerations in Nerve Conduction Studies- The Clinical Neurophysiology Primer2007, pp 217-227

47. Nicholas A. Boon Et al – Davidson's Principles & Practice of Medicine – 20th ed – pages 744- 762

48. Fadel BM et al - Hyperthyroid heart disease- Clin Cardiol. 2000 Jun;23(6):402-8.

49. Sheldon S. Waldstein - A clinical study of thyroid storm- Ann Intern Med. 1960;52(3):626-642

50. Anthony P. Weetman - Graves' Disease: N Engl J Med 2000; 343:1236-1248 October 26, 2000

51. Miho Inoue: Hyperthyroidism during pregnancy- Canadian Family Physician July 2009 vol. 55 no. 7 701-703

52. Fauci et al - Harrison's Principles of Internal Medicine – 17 th ed –pages 2224-2247

53. Michael B Zimmermann Iodine-deficiency disorders – The LANCET - Volume 372, Issue 9645, 4–10 October 2008, Pages 1251–1262

54. Elisabeth Hyjek et al - Primary B cell lymphoma of the thyroid and its relationship to Hashimoto's Thyroiditis- Human Pathology Volume 19, Issue 11, November 1988, Pages 1315–1326

55. Lazarus JH et al- Thyroid disease in pregnancy and childhood.- Minerva Endocrinologica :2005, 30(2):71-87

56. Walter G Bradely - Neurology in clinical practice - 4th ed 1062-64 , 1078-79

57. Donald McEachern- the relationship of hyperthyroidism to myasthenia gravis- The Journal of Clinical Endocrinology & Metabolism- Volume 8 Issue 10 - October 1, 1948.

58. V Sahni et al - Thyrotoxic Neuropathy- An Under Diagnosed Condition - Med J Malaysia Vol 62 No 1 March 2007

59. Irwin Klein - Hypothyroidism presenting as muscle stiffness and

pseudohypertrophy:Hoffmann's syndrome - The American Journal of Medicine Volume 70, Issue 4, April 1981, Pages 891–894

60. John Walton -Brain,'s Diseases of the Nervous system-10 th ed -pages-137,547,616,653- 54

61. Maynika V Rastogi - Congenital hypothyroidism - Orphanet Journal of Rare Diseases 2010, 5:17

62. Moinuddin H. Mokhashi - Hyperthyroidism in children - The Indian Journal of Pediatrics September 2000, Volume 67, Issue 9, pp 653-656

63. Ambika Gopalakrishnan Unnikrishnan et al, - Thyroid disorders in India: An epidemiological perspective - Year : 2011 | Volume : 15 | Issue : 6 | Page : 78-81

64. Juan Bernal - Thyroid Hormones in Brain Development and Function-Thyroid Disease Manager- Last Updated: December 1 7 , 201 2

65. Wilmar M. Wiarsinga et al - Adult hypothyroidism - Thyroid Disease Manager - updated march 28 201

66. Song TJ et al - The prevalence of thyrotoxicosis-related seizures. Thyroid. 2010 Sep;20(9):955-8

67. Pooja Pothiwala et al - Analytic Review: Thyrotoxic Periodic Paralysis: A Review - J Intensive Care Med March 2010 vol. 25 no. 2 71-77

68. Harold F. Dunlap et al - A syndrome resembling familial periodic paralysis occurring in the course of exophthalmic goiter – ENDOCRINOLOGY Volume 15 Issue 6 - November 1, 1931

69. Cesar H. Magsino, JR et al - Thyrotoxic Periodic Paralysis - South Med J. 2000;93(10)

70. Fisher M et al - Pyramidal tract deficits and polyneuropathy in hyperthyroidism, Combination clinically mimicking amyotrophic lateral sclerosis - Am J Med. 1985 Jun;78(6 Pt 1):1041-4

71. Lai CL et al - A central nerve conduction study in hypothyroidism: before and after thyroxine replacement - Kaohsiung J Med Sci. 1998 Dec;14(12):743-50

72. Ozata M - Evaluation of central motor conduction in hypothyroid and hyperthyroid patients - Journal of Endocrinological Investigation [1996, 19(10):670-677]

73. Hala S Sweed et al - Cognitive and Neuromuscular Assessment in Geriatric Patients with Thyroid Dysfunction -Egypt J. Neurol. Psychiat. Neurosurg., January 2007 Vol.44 Issue : 1 page 237-250

74. Chiou-Lian Lai et al - A longitudinal study of central and peripheral nerve conduction in hypothyroid rats - Journal of the Neurological Sciences Volume 148, Issue 2 , Pages 139-145, 29 May 1997

75. Ihsan M. Ajeena et al - Prevalence of Neuromuscular Abnormalities in Newly Diagnosed Patients with Thyroid Dysfunction - American Journal of Research Communication 2013: Vol 1 (3)

76. Yeasmin Set al-Sensory Neuropathy in Hypothyroidism: Electro physiological and Clinical Findings - J Bangladesh Soc Physiol. 2007

Dec;(2): 1-6.

77. V. Reid - Hypothyroidism presenting as recurrence of previously surgically decompressed carpal tunnel syndrome - Grand Rounds Vol 5 pages 26–27 Speciality: Endocrinology, General surgery

78. Nebuchennykh, M et al - European Journal of Neurology Volume 17, Issue 1, pages 67–72, January 2010

79. El-Salem et al - Neurophysiological Changes in neurologically asymptomatic hypothyroid patients: A prospective cohort study - Journal of Clinical Neurophysiology: December 2006 - Volume 23 - Issue 6 - pp 568-572

80. Gulbun Yuksel - Nerve Conduction Studies, SEP and Blink Reflex Studies in Recently Diagnosed,Untreated Thyroid Disease Patients - Journal of Neurological Sciences [Turkish] 24:(1)# 10;7-15, 2007

81. Sabina Yeasmin - Motor Neuropathy in Hypothyroidism: Clinical and Electrophysiological Findings - BSMMU J 2008; 1(1): 15-18

82. Ruurd F Duyff - Neuromuscular findings in thyroid dysfunction: a prospective clinical and electrodiagnostic study - J Neurol Neurosurg Psychiatry 2000;**68**:750–755

83. SH Jalilzadeh et al - Peripheral Nerve Function in Subclinical Hypothyroidism: A Case-Control Study -International Journal of Endocrinology and Metabolism – 2006 : Volume 4, Issue 2, Page: 78 - 83

84. Sachin Pawar et al **-** Usefulness of blink reflex in hypothyroid patients with

or without polyneuropathy : A case control study - 56 Pawar, Udan, Jain, Shende and Singh Indian J Physiol Pharmacol 2014; 58(1)

85. Ian D. Ramsay et al - electromyography in thyrotoxicosis - Quarterly Journal of Medicine, New Series XXXIV, No. 135, July 1965

86. Adhikesavan et al - A study of nerve conduction velocity in newly diagnosed hypothyroid females- world journal of medical sciences9 (4) :198-201 , 2013

87. Khedr EM et al - Peripheral and Central nervous system alterations in hypothyroidism: Electrophysiological findings-Neuropsychobiology .2000 Jan 41(2) :88-94

88. Marcia W Cruz et al - Electroneuromyography and neuromuscular findings in 16 hypothyroid patients: Arq Neuropsiquiatr 1996 -54(1):12- 18.

PROFORMA

Name: Age/Sex:

Address: Personal habits:

Ht/Wt:

Present complaints:

Past History:

Diabetes, Hypertension, neurological disorder, drug intake and Rheumatoid disorder.

General Examination:

Pallor clubbing cyanosis edema jaundice

PULSE **BP:** **RR:**

NECK EXAMINATION:

SYSTEMIC EXAMINATION:

CVS:

RS:

CNS:

ABDOMEN

Provisional diagnosis:

Investigations:

Hb: TC: DC: ESR:

RBS: Bl.Urea: S.creatinine:

Liver function tests Serum Calcium:

Thyroid function tests: FT3: FT4: TSH

Nerve conduction study results:

NERVE	Latency	AMPLITUDE	CV	F Wave latency
SURAL SENSORY				
MEDIAN SENSORY				
ULNAR SENSORY				
TIBIAL MOTOR				
MEDIAN MOTOR				
ULNAR MOTOR				

CONSENT FORM

DR.K.Balasubramaniam, Postgraduate student in the department of physiology, Tirunelveli Medical College, Tirunelveli is studying the effect of Thyroid disorders on nerve conduction studies. The test procedures are

1. Sensory conduction study of upper and lower limbs.
2. Motor conduction studies of upper and lower limbs.

The procedure was explained to me clearly. I understand that there are no risks involved in the above procedures. I hereby give my consent to participate in the study. The data obtained may be used for research and other publication purpose.

Name :

Place :

Signature :

Normal Group

S.No	Age	TSH	sensory									motor										
			sural			median			ulnar			post tibial				median				ulnar			
			Latency	CV	AMP	Latency	CV	AMP	Latency	CV	AMP	DL	CV	AMP	F Wave La	DL	CV	AMP	F wave La	DL	CV	AMP	F wave Lat
1	42	3.4	3.92	42.8	6.2	3.08	52.18	21.2	3.15	51.2	18.2	5.82	43.4	3.6	46.48	3.92	49.86	5.2	24.32	2.8	50.2	6.4	25.38
2	38	3.2	4.12	44.3	6.8	2.88	54.2	23.6	3.32	53.28	17.4	5.45	42.62	3.78	47.28	3.87	52.18	4.26	24.86	2.6	52.8	6.2	24.32
3	28	2.6	3.82	43.96	7	3.2	53.86	20.2	3.26	52.46	17.6	6	46.48	3.85	47.84	3.68	51.28	4.4	23.86	3	51.44	6.32	25.78
4	43	2.4	3.74	42.82	5.9	2.67	50.4	22.6	3.47	49.1	17.3	5.92	44.72	3.45	46.38	4.1	53.88	4.26	23.68	3.02	50.28	6.1	26.32
5	34	1.8	4.16	41.92	6.3	2.98	51.26	20.7	3.28	50.48	19.1	5.64	42.36	3.74	46.94	3.68	51.92	4.32	24.32	2.67	51.34	6.02	26.1
6	49	1.1	3.72	44	6.6	2.86	53.42	22.3	3.46	50.1	17.3	5.98	42.78	3.44	47.8	3.88	49.82	4.38	23.84	2.46	52.18	5.9	24.92
7	38	2.3	4	42.83	6.1	2.66	52.8	21.4	3.28	51.24	18.3	5.68	45.6	3.78	47.48	4.48	48.88	4.92	22.96	2.84	53.56	6.26	25.48
8	43	2.5	4.24	38.82	6.5	3.24	48.4	19.4	3.56	49.48	17.3	5.82	44.48	3.24	45.32	4.12	51.26	3.88	23.62	3.1	52.48	6.52	24.98
9	37	2.7	4.16	41	6.4	3.02	51	21.4	3.48	50.4	16.9	5.64	45.36	3.84	47.28	4.28	54.28	4.32	23.48	3.24	50.13	6.41	25.32
10	21	1.6	3.62	39.92	6.8	2.74	52.6	23.1	3.36	51.6	17.8	5.66	42.84	3.62	46.6	4.14	50.28	4.24	24.8	3.12	50.28	6.48	25.62
11	37	3.1	3.34	43	6.2	2.82	53.62	20.2	3.7	49.4	18.1	5.96	41.83	3.56	48.26	3.76	51.46	4.52	22.34	3.43	48.74	6.3	24.88
12	45	1.7	4	44.92	5.6	2.72	52.14	20.6	3.21	53.2	19	5.5	42	3.14	47.82	4.22	51.7	4.32	22.96	3.5	48.34	5.8	24.64
13	28	2.9	4.16	40.9	5.8	3.32	49	19	3.3	50.46	17.4	6.2	40.12	2.88	47.6	4.24	54.52	4.12	24.28	3.28	49.42	6.29	24.92
14	36	3	3.86	42.82	6.1	3.11	50.58	18.7	3.5	51	17.1	5.78	41.82	3.18	47.4	4.52	47.92	4.24	24.64	3.16	52.18	6.28	24.83
15	34	3.2	3.58	41.6	6	3.2	49.48	20.2	3.45	52.45	19.4	5.76	43.46	3.62	46.4	3.32	49.98	4.54	24.84	2.98	53.43	6.32	25.64
16	26	2.6	4.24	40	6.2	3.14	50.2	21.3	3.4	57.62	18.2	6.02	44.37	3.36	47.3	4.26	50.32	4.62	24.9	2.76	51.53	6.18	25.8
17	44	2.4	4.38	40.86	5.4	3.2	51.6	22.5	3.74	51.24	17.3	6.14	40.87	3.38	47.9	4.32	51.96	4.72	23.82	2.76	52	6.24	24.9
18	29	3.2	4.12	44.58	6.3	3.2	52.34	20.1	3.46	50.08	18.5	6.06	43.48	3.23	47.26	3.68	53.38	4.21	24.62	2.82	53.38	6.32	24.92
19	24	1.2	3.68	45.6	6.7	3.12	50.06	20.4	3.24	50.4	17.4	5.76	42.46	2.64	46.38	4.23	50.68	4.45	24.88	2.94	51.65	6.54	25.24
20	33	1.1	4.32	40.8	5.7	2.99	51	21.3	3.98	50.14	17.9	5.42	44.58	3.58	47	4.64	46.4	4.28	23.74	3.18	53.32	6.3	25.86
21	47	2.7	4.21	41.25	5.6	3.06	50.28	23.2	3.43	50.12	18.3	5.54	43.86	3.22	48.2	3.34	50.04	4.26	22.96	3.16	49.47	6.23	26.32
22	36	3.4	3.86	41.36	6.6	2.83	50.4	22.4	3.56	49.82	17.2	5.95	47.8	3.98	47.48	4.38	49.82	4.32	24.92	3.2	48.8	6.42	25.34
23	27	3.2	3.98	42.89	6	2.94	51.38	23.6	3.26	48.78	18.4	5.64	45.56	3.75	47.9	4.28	51.62	4.29	25.18	2.68	49.45	6.35	25.61
24	44	2.2	3.82	43.52	6.1	2.8	50.28	22.5	3.18	52	17.5	6.23	38.78	3.35	47.9	3.86	50.64	4.51	24.2	2.96	49.5	5.52	26.48
25	50	2.1	4.28	38.56	6.2	3.12	53.22	21.9	3.25	51.4	17.3	6.08	45	3.16	47.44	3.59	51.38	4.32	24.48	3.2	52.72	6.1	27

CV : Conduction Velocity
AMP : Amplitude (μV For sensory, mV for Motors Conduction Studies)
DL : Distal Latency
F Wave Lat : F Wave Latency

Hypothyroid Group

S. No	Age	Dura	TSH	sensory									motor										
				sural			median			ulnar			post tibial				median				ulnar			
				Latency	CV	AMP	Latency	CV	AMP	Latency	CV	AMP	DL	CV	AMP	Fwave lat	DL	CV	AMP	F wave lat	DL	CV	AMP	F wave Lat
1	35	3	20.8	4.1	44.46	6.36	3.1	41	13.87	3.4	50	18	5.64	40.8	3.48	47.18	4.2	49.2	4.1	23.28	3.1	50.4	7.1	24.92
2	27	18	49	3.88	42.78	6.1	3.65	34	14.63	3.45	50.28	16.4	6.23	39.68	4.26	48.12	6.23	48.86	4.3	24.2	2.8	59.1	6.4	25.24
3	48	21	29.2	5.32	33.74	5.82	3.58	38	16.48	4.26	51.06	17.3	6	41.2	2.4	48.2	4.4	49	4.3	24.46	2.8	51	4.2	25.86
4	25	12	64	5.62	30.88	5.92	3.7	34.56	17.28	4.1	44.4	18.3	6.12	39.28	2.4	47.48	5.32	50.01	2.9	23.62	3.1	49.2	6.8	26.48
5	41	2	15	3.8	42.3	6.14	2.98	51.24	20.1	3.5	50.9	19.2	5.6	41.3	3.66	47.9	4.23	49.32	4.3	22.82	2.9	49.21	6.4	25.42
6	36	9	56.1	5.4	31.87	4.86	3.06	58.6	21.48	4.28	44	15.9	5.63	39.78	2.2	48.12	5.68	49.2	4.1	22.48	3.2	51.14	6.12	24.68
7	25	5	9.3	4.01	47	6.08	3.1	50.24	19.4	3.5	50.01	20.1	5.48	41.2	4.1	48.2	4.1	49.48	4.4	24.3	2.8	49.12	6.1	24.62
8	29	24	43	4.86	40.38	5.28	4.2	33.5	12.8	3.36	51.6	20.2	5.28	42.87	2.7	47.48	5.32	50.1	4.2	23.8	3	49	7.1	24.34
9	22	15	55.4	4.9	33.67	4.98	3.78	41.6	14.26	3.96	48	21	6.1	38.28	2.6	46.26	4.1	49	2.1	23.64	3.31	42.6	4.3	25.38
10	44	12	35.2	4.46	38.76	5.68	3.36	52.8	20.48	4.02	47.52	14.3	5.86	46.5	2.6	46.8	4.3	50	4.4	23.48	3.1	50.8	6.8	24.32
11	42	18	18.3	4.34	40.48	5.82	3.38	47.28	16.48	3.3	50	16.2	6.2	40.98	3.7	47.4	5.92	46.2	5.1	24.8	3	50	6.2	24.98
12	38	21	36	4.74	33.86	5.2	3.04	59.4	21.65	2.8	55.2	17.8	6.86	39.5	3.9	48.26	4.3	49.4	4.2	22.34	3.2	50.12	6.2	25.86
13	45	9	52	5.21	42	6.12	3.86	33	15.4	3.98	47.2	19.6	5.9	42	2.6	47.82	4.32	47.2	2.8	22.96	2.9	51.21	4.2	25.4
14	20	7	69	4.08	35.48	5.12	3.26	48.3	21.34	3.67	48.53	14.4	6.1	41.2	2	47.6	5.38	49.8	4.4	24.3	3.4	48.82	6.5	24.94
15	37	18	42.1	4.1	42.78	6.32	3.76	37.86	18.86	3.4	52.1	17.2	5.9	42	2.8	47.4	3.8	49.6	4.1	23.38	2.6	50.31	4.2	24.66
16	40	3	23	3.46	43.56	6.28	2.92	54.6	17.86	3.45	50.23	13.4	6	42	3.72	48	4.2	50.1	4.2	24.32	2.3	50.2	6	25.83
17	49	4	19	3.92	42.36	6.41	3.31	48.38	26	3.88	48.23	18.7	7.9	37.8	3	47.38	4	49.9	4.3	24.86	2.4	51.3	6.02	25.9
18	36	8	51	4.93	32.56	5.08	3.38	42.28	20.5	3.68	46.05	16.2	5.88	41.2	4.6	46.94	6.1	48.8	4	23.86	3.1	50	6.4	25.46
19	22	10	22	4.21	39.96	6.03	3.86	47	13.85	2.96	50.16	15.3	6.12	41.54	2.8	47.8	4.42	43.2	4.2	23.68	3.2	45.38	6	26.38
20	30	6	31	4.16	42.6	5.96	2.67	50.27	16.6	3.34	50.4	17	5.4	41.28	3.86	47.48	3.6	50.06	4.1	24.28	2.9	49	6	26.74
21	31	21	16	4.2	42.48	6	4.16	47.6	16.65	3.02	41.28	18.2	6.1	39.76	2.8	46.92	6	47.82	4.3	24.82	2.4	49.26	6.7	26.4
22	41	11	57	5.46	30.56	4.94	3.91	38.78	15.82	3.96	46.8	15.2	6.86	32	4	46.1	4.55	48.12	3.1	26.32	3	49.12	6.1	24.62

Dura: Duration in months

CV : Conduction Velocity

AMP : Amplitude (μV For sensory, mV for Motors Conduction Studies)

DL : Distal Latency

F Wave Lat : F Wave Latency

HYPERTHYROID GROUP

Sl.No..	age	Dura	TSH	sensory									motor										
				sural			median			ulnar			post tibial				median				ulnar			
				Latency	CV	AMP	Latency	CV	AMP	Latency	CV	AMP	DL	CV	AMP	F wave lat	DL	CV	AMP	F wave lat	DL	CV	AMP	F wave lat
1	21	15	0.12	4.92	40.82	5.1	2.68	50.2	19.4	4.2	48.45	16.8	6.4	39.2	3.8	48.26	3.82	48.2	5	23.86	2.68	52.12	6.8	25.38
2	33	4	0.23	3.64	40.1	6.3	3.1	45.6	18.82	3.5	49.31	15.82	6.2	40	3.72	47.82	3.66	54.2	4.62	23.68	3.33	50.8	6.48	25.46
3	23	12	0.1	4.92	40.38	4.68	3.9	50.2	20.34	3.92	51.2	17.2	5.4	42.6	2.89	47.6	3.34	48.98	2.48	24.28	3.41	47.6	3.1	24.48
4	40	2	0.08	5.92	36.38	5.38	3.58	46.8	17.8	3.42	49.4	16.62	6.1	38.8	2.69	47.4	4.12	48.3	4.8	22.96	2.82	50.46	6.12	25.92
5	43	9	0.16	5.76	38.58	6.01	4.58	46.58	21.2	4.42	52.4	18.8	5.28	38.6	2.58	47.24	5	52.4	4.2	24.92	2.57	50.1	6.8	24.82
6	32	18	0.24	4.94	40.28	4.98	4	48.48	16.4	3.82	47.78	14.3	5.68	41.6	2.73	46.26	4.02	53.4	2.5	25.18	2.86	50.22	6.1	24.68
7	24	3	0.26	3.5	44.62	6.12	2.8	50.51	21.6	2.86	50.48	17.8	6.1	38.6	3.9	47.12	4.14	44.36	4.6	24.2	3.3	50.48	6.21	26.24
8	34	21	0.14	4.91	38.48	5.86	2.98	50.2	15.8	4.28	42	16.46	5.52	41.2	2.2	47.32	3.45	47.4	4.48	24.46	3.26	47.82	4.12	25.34
9	46	15	0.25	4.96	40.42	4.18	3.1	45.42	17.48	2.91	51.28	18.2	6.18	41	2.65	47.18	4.42	46.3	4.1	23.98	2.54	52.38	7	24.98
10	27	10	0.06	4.02	45.83	6.4	4.29	46.82	19.4	3.5	48.78	15.27	5.1	39.36	3.65	48.12	3.82	49.21	4.23	24.26	3.21	51.65	6.1	24.63
11	47	3	0.18	5.21	38.68	3.72	4.48	45.81	18.42	3.99	49.2	16.62	6.1	40.98	3.62	48.2	4.12	48.8	2.2	25.16	3.32	48.86	2.98	25.34
12	35	11	0.21	5	38.92	5.15	4.3	48.6	16.28	3.8	47.68	15.42	5.28	41.78	2.36	47.48	4.38	47.3	4.3	24.38	3.3	47.82	6.5	25.61
13	42	15	0.2	5.43	38.76	5.46	3	51.6	21.61	3.16	51.28	17.2	5.9	38.92	2.98	47.9	3.18	54.3	3.6	24.16	3.38	52.3	7.1	25.4
14	25	12	0.28	4.86	39.86	5.12	3.68	46.48	17.68	3.73	47.98	16.3	6.62	36.42	3.7	47.9	4.36	56.3	4.6	22.37	3.28	51.28	6	24.9
15	26	18	0.22	4.12	43.48	6.2	2.88	51.78	20.18	3.2	50.28	17.5	6.32	38.87	3.28	46.23	6.28	48.3	4.32	23.48	3.3	48.28	6.1	26.84
16	39	24	0.1	4.98	39.63	5.38	4.2	47.68	19.28	3.79	49.76	16.7	6.32	39.46	3.15	48.1	3.2	52.8	4.1	24.8	3.26	48.87	6.66	26.1
17	43	5	0.24	3.98	43.8	6.14	2.6	50.78	20.4	2.98	51.4	17.3	5.3	41.26	3.92	48	4.4	45.4	4.21	22.34	3.32	50.52	6.1	24.92
18	45	18	0.18	4.82	40.42	5.1	4.3	50.48	17.78	4.72	46.6	16.43	6	42.6	1.6	46.9	5.32	48.7	4.64	22.96	2.9	52.38	6.9	25.24

Dura : Duration in Months
CV : Conduction Velocity
AMP : Amplitude (μV For sensory, mV for Motors Conduction Studies)
DL : Distal Latency
F Wave Lat : F Wave Latency